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THESIS

Suicidality in the Perinatal Period.

Results of PND-ReScu Study

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FOREWORD

'Why Mothers Die 2000-2002' (Lewis & Drife, 2004), highlighted suicide as a major cause of maternal death, and, like the 1997-1999 CEMD report (Lewis & Drife, 2001, 2004), found suicide to be the leading cause of indirect or late-indirect deaths for the year following delivery. The majority of these deaths appeared to be of women suffering from psychosis or a very severe depressive illness.

Although the majority of new onset and recurrent disorders related to childbirth are mood disorders, we also seek to address the growing realisation that anxiety disorders are both prominent and have an adverse effect on child development (Rambelli et al., 2009; O'Connor et al, 2002).
In addition, women with other psychotic, non-psychotic and personality disorders will become pregnant and require managing throughout pregnancy and after delivery.

In our experience, it is essential to approach the management of women with perinatal psychiatric disorders from a bio-psychosocial perspective and for health professionals to be fully aware of the sociocultural context and the 'meaning' of this illness for the mother and her family.

INTRODUCTION

Suicide: a Public Health Issue

Suicide and self-inflicted injuries are leading causes of injury-related deaths worldwide. There are an estimated 10-20 million attempted suicides each year and one million completed suicides (WHO. Fact Sheet No 217. The newly defined burden of mental problems, April 1999). Moreover, suicide has become recognized as a serious public health problem that is causing concern, particularly in the European Union (EU). Suicide has been recognized since early civilization. Hanging was a method frequently used before such tools as knives became commonplace. Attitudes toward suicide have shifted through the centuries as people gave names to feelings like shame and guilt (van Hooff, 2000). Suicide is now seen as an act with complex motivation and many contributing factors. It occurs in every culture, although at widely differing rates, and is affected by cultural practices, expectations, and values.

Suicidal behaviour spans a spectrum that, in addition to completed suicide, also encompasses suicidal ideas and thoughts of varying intensity and specificity, and other acts of deliberate self-harm of varying intent and lethality. Silverman and colleagues (2007) have proposed the definitions listed below:

Suicidal Behaviors

Suicide is a deliberate act of self-harm with at least some intent to die that results in death. Suicide attempt is a deliberate act of self-harm with at least some intent to die that does not result in death. Such acts have a wide range of medical seriousness.

Suicidal Thoughts

Suicidal ideations are thoughts of attempting suicide. Such thoughts have a wide range of specificity, intensity, and frequency.

Suicide plans are a severe form of suicidal ideation that include identifying a method or scenario to attempt suicide.

Nonsuicidal Thoughts and Behaviors

Death ideations are thoughts of dying but without ideas for suicidal behavior per se. Nonsuicidal self-injurious behaviors are self-directed acts of self-harm without intent to die. Broadly, these acts tend to have intrapersonal (e.g., manage emotion) or interpersonal (e.g., communicate distress) motivations and include a variety of behaviors (cutting, piercing, burning) and a wide range of medical seriousness.

Gender Issues in Suicide Risk

In the developed Western countries the number of men committing suicide is three times more than that of women. However, women are more likely to attempt suicide than men (Kaplan and Sadock, 2003). This is not a recent phenomenon, as in the nineteenth century Durkheim (1897) pointed out a similar gap in suicide mortality among men and women; but the difference became more apparent in the last decades of the twentieth century.

According to the 'gender paradox' (Canetto and Sakinofsky, 1998), suicide attempts are more common among females compared to males (female/male ratio: 4-6/1), which lead the researchers to believe that male gender can be classified as a special, tertiary risk factor for suicide in the hierarchical classification of suicide risk factors characterised by Rihmer (Rihmer et al., 2002). Paradoxically, the higher number of suicide attempts tend to lower the risk of fatal outcome among women.

Completed and attempted suicides are not different phenomena, and many times often the reasons, the mechanisms and the methods are the same in both cases, only the outcome differs.

Since gender is one of the most frequently replicated predictors for suicide, gender differences in suicidal behaviour have been analysed in a number of recent studies (Hawton, 2000; Canetto and Sakinofsky, 1998; Moscicki, 1994).

The main hypotheses to explain the higher suicide mortality in men and the higher number of suicide attempts in woman, are:

a) **Socio-economic factors:** many studies indicated that socio-economic risk factors for suicide also differ among males and females (Canetto and Sakinofsky, 1998). Unemployment, retirement, single lifestyle and absence from work due to sickness are the most significant risk factors for suicide, mainly among males than in females (Qin et al., 2000; Hawton, 1998). It seems likely that unemployment and uncertainties at work would have a stronger impact on the male population's self-esteem and mental stability, while women have more possibilities to retain other status and domestic and caring responsibilities (Payne et al., 2008; Varnik et al., 1998). Male status is more often dependent on success at the workplace and control over their work and financial background, so they may be more sensitive to deprivation and more

vulnerable to the basic gender-role distress.

b) **Socio-biological factors:** from a socio-biological viewpoint there are some age-dependent gender differences, which might be in connection with the diminished capacity to reproduce and to get social support. In many countries (e.g., United States, Hungary) suicide rates in women tend to peak around middle age (the years of the menopause and the 'middle life crisis'), while male suicide rates are much more higher among the elderly (Fekete et al., 2005). In old age, men become less fit physically and the reproductive capacity diminishes with isolation and deteriorated social support (Maris, 2002). Urban living is linked to a higher rate of female suicide, mostly because women living in cities feel more alienated and socially isolated (Murphy, 1998).

c) **Methods:** concerning the differences between various methods, males tend to use more violent methods both in completed and attempted suicide, while women are more likely to choose self-poisoning (Kaplan and Sadock, 2003). A recent European multicentre study on youth suicide showed that males have a significantly higher risk for using firearms, hanging and poisoning by other means in their suicide attempts and lower risk of poisoning by drugs and jumping (Varnik et al., 2008). The difference between the rates of suicide attempts and completed suicides among women may reflect a lesser degree of intent, but it also shows a tendency among women not to use highly violent or particularly lethal methods. Greater suicidal intent, aggression, knowledge regarding violent means, less concern about bodily disfigurement are all likely explanations for the excess of violent suicide in males (Hawton, 2000).

d) **Cultural beliefs**: strong cultural beliefs of suicide considered as 'masculine' and surviving a suicide as being culturally unacceptable might influence young males to use more violent or lethal methods (Mittendorfer-Rutz, 2006). The excess rate of suicide attempts in females, and the stronger association between attempted and completed suicide in males (Hawton, 1998) refer to the fact that attempts by females are more often based on nonsuicidal, but communicative motivation, while in males the attempts are often associated with greater suicidal intent; so they tend to choose methods without regarding their attractiveness (Payne et al., 2008).

e) **Mental illnesses:** they are the most replicated predictors for suicides among both genders but especially for women (Rihmer et al., 2002). Psychological autopsy studies clearly demonstrate that affective disorders carry the highest risk, both to males

and females, often comorbidly with personality-disorders and with other mental disorders (Hawton, 2000). Rates of schizophrenia and addictions are higher among males, while eating disorders - especially anorexia nervosa- are more common among female suicide victims (Mortensen et al., 2000; Harris and Barraclough, 1997;). In a longitudinal study**, hospitalised mental illness** (particularly recent discharge from a psychiatric hospital) appeared to be the most prominent risk factor for suicide with both genders (Qin et al., 2000). These differences may be viewed as artifacts of men's lower likelihood to seek help or because the symptoms of male depression are different from women's. If the symptoms of a mental disorder are perceived as inconsistent with masculinity, men try to hide such symptoms (as signs of weakness) and do not ask for treatment (Payne et al., 2008). Men in line with norm-congruent behaviour drink more and more alcohol to combat depression instead of seeking professional help. Furthermore, alcohol and substance abuse, in its own right, has positive associations with suicide, especially among women (Payne et al., 2008).

f) **Protective factors:** in spite of the fact that little research attention has been paid to factors which protect against suicide, there are some differences even among the protective factors. According to a Danish study, **parenthood** appears to explain an apparent protective effect of marriage for women, rather than the marriage itself per se, whereas among men marriage appears to be a protective factor in its own right (and single status is a risk factor) (Qin et al., 2000). Single men have higher risk for suicide than single women, and divorce or the death of a spouse is a significant risk factor for men, but not for women (Qin et al., 2003; Louma and Pearson, 2002) who are more likely to have extended and rooted social networks which might help them to cope with interpersonal losses (Payne et al., 2008). Finally, **pregnancy** has been found to be a protective factor for women (Appleby, 1996) such as the caring for children (Payne et al., 2008).

g) **Help-seeking attitude:** females are also more likely to seek help from general practitioners for their mental health problems (Osvath, Michel, Fekete, 2003). Men often view help-seeking as a sign of weakness (Murphy, 1998), they rarely ask for professional help and they are also more reluctant to ask for support from family and friends (Biddle et al., 2004). This reluctance and the special features of male depression may contribute to the fact that depression is more often undetected and untreated

among men (Rihmer et al., 2002). This may -at least partially- explain the striking paradox: major depression (which has the strongest association with suicide among mental disorders) is about twice as common among women than men, but men are four times more likely to commit suicide than women.

h) **Compliance:** several studies and summarised clinical impressions suggest that the compliance for the therapy and prevention of male patients is significantly poorer than for females, and there is also some indication from treatment studies that fewer male attempters actually benefit from the treatments offered to them (Hawton 1998, 2000). While this may reflect differences in the overall attitude towards help, it could also result from the available therapy type. Gender differences in verbal abilities and the reluctance of many males to share emotional problems may make some of the usual talking therapies less attractive to some males, at least initially (Hawton 2000). These data suggest that gender-specific suicide prevention could be further improved by diagnosing and treating the male patients' mental problems in a more effective manner, since they often mask their problems with impulsive, aggressive behaviour or alcohol abuse and their behaviour is frequently characterised by a lack of help- seeking attitude and noncompliance (Rihmer et al. 2002).

In the complex socio-cultural model the traditional gender roles have a close relationship with suicide-related behaviour and the socio-cultural factors impact and reinforce these. Male gender role (characterised by dominance, aggressiveness, invulnerability) can help to explain the reason why men tend to choose more lethal methods, why they are struggling with asking for help and support for psychological problems and mental disorders, and why they tend to misuse alcohol and other substances as inappropriate self-medication. In contrast, traditional female role typically includes fragility, emotionality, expressiveness and family orientation, which may explain women's help-seeking behaviour and their tendency to use less lethal methods. Additionally women have more opportunities to cope with negative life-events in a more effective manner (Payne et al. 2008).

While comparing rates of suicide and attempted suicide -according to gender and **age groups**- it is well recognised that suicides show almost a linear increase in both genders. The number of attempts has **three different peaks** parallel in both sexes. The

first peak is the young-aged group (around the twenties), at the time of adolescent crisis; the second is the middle-aged group (around the forties), in the years of the mid-life crisis; and the third peak is the oldaged group (around the eighties), at the time of life-end period. The association of significant life periods of the psychosocial developmental crisis (Erikson 1950) and the age curve of suicide attempts emphasise the importance of psycho-socio cultural origin of suicidal behaviour. Suicide attempts are very high in the groups of young males, and young and middle-aged females, thus indicating a more important communicative aspect (asking for protection from others in the crisis situation) of these acts.

- A woman takes her own life every 90 minutes in the U.S., but it is estimated that one woman attempts suicide every 78 seconds.
- Women attempt suicide three times as much as men.
- The higher rate of attempted suicide in women is attributed to the elevated rate of mood disorders among females, such as major depression, dysthymia and seasonal affective disorder.
- Although women attempt suicide more often, men complete suicide at a rate four times that of women.
- Firearms are now the leading method of suicide in women, as well as men.
- Suicide is more common among women who are single, recently separated, divorced, or widowed.
- The precipitating life events for women who attempt suicide tend to be interpersonal losses or crises in significant social or family relationships.
- Many women who suffer from manic-depressive illness experience their first episode in the postpartum period.
- Sixty percent to 80 percent of women experience transient depression, and 10 percent to 15 percent of women develop clinical depression during the postpartum period.
- The suicide rates for men rise with age, most significantly after age 65.
- The rate of suicide in men 65+ is seven times that of females who are 65+.
- The suicide rates for women peak between the ages of 45-54 years old, and again after age 75.
- Women are more likely than men to have stronger social supports, to feel that their relationships are deterrents to suicide, and to seek psychiatric and medical intervention, which may contribute to their lower rate of completed suicide.

American Foundation for Suicide Prevention, 2011.

CO-OCCURRING MENTAL DISORDERS AND SUICIDAL BEHAVIOR

Co-occurring mental and substance use disorders are a common and potent combination among those who die by suicide. An exhaustive review of psychological autopsy studies conducted internationally showed that mood disorders (particularly major depression) and substance use disorders were the most common disorders in people who died by suicide, and that 38 percent had a substance use disorder(s) plus one or more other psychiatric disorder(s) (Cavanagh et al., 2003). A wealth of data illustrate that this combination also confers risk for attempted suicide (e.g., McCloud, Barnaby, Omu, et al., 2004; Yen et al., 2003).

Mood Disorders

About 60% of the approximately 30,000 deaths from suicide each year occur in people with major depression, and increased rates of prescriptions for selective serotonin reuptake inhibitors (SSRIs) and other new-generation non-SSRIs are associated with lower suicide rates both between and within countries over time (Gibbons et al., 2005). A meta-analysis and literature review has shown that suicide occurs in patients with major depression 20.4 times more frequently than in the general population, based on a comparison using standardized mortality ratios (SMRs) (Harris and Barraclough, 1997). A study of trends in suicidal ideation, suicide, suicidal plans and gestures, and suicide attempts in the United States has shown that despite a dramatic increase in treatment between 1990-1992 and 2001-2003, there has been no significant decrease in suicidal thoughts and suicide plans, gestures, or attempts (Kessler et al., 2005). A study of completed suicides found that of the 75% of patients who had an affective disorder, 70% had received psychiatric care within 1 year of their suicide and 51% had received care within 1 month of their suicide (Robins, 1981). A study in Finland showed that 75% of the individuals who committed suicide had a history of psychiatric treatment, and 45% were receiving active treatment at the time of death. Only 3% had received antidepressants in adequate dosages, 7% had received weekly psychotherapy, and 3% had received electroconvulsive therapy (Isometsa et al., 1994).

Mood disorders commonly co-occur with substance use disorders and confer significant risk for suicidal behavior (Conner et al., 2003; Darke and Ross, 2002;

Dhossche, Meloukheia, Chakavorty, 2000; Preuss et al., 2002; Roy, 2001, 2002). Major depressive episode (MDE), in particular, is associated with suicidal behavior. Among adults with a past year diagnosis of MDE, those who reported past month binge alcohol use and/or illicit drug use were more likely to report past year suicidal ideation and suicide attempts than those who did not (Office of Applied Studies, 2006). Moreover, whether or not depression is induced by a substance use disorder or occurs independent of substance use, it confers risk for suicidal behavior among individuals with substance use disorders (Aharonovich, Liu, Nuneset al., 2002; Preuss et al., 2002). In other words, it is essential that substance-induced depression not be dismissed or minimized by providers because this type of depression confers risk, as does independent depression.

Bipolar Disorder

Bipolar manic-depressive disorders are prevalent, often severe and disabling, major psychiatric illnesses found worldwide (Goodwin and Jamison, 2007; Tondo and Baldessarini, 2005; Tondo et al., 2003). Bipolar disorder presents elevated risks of premature mortality due to adverse outcomes of medical disorders, accidents, and complications of commonly comorbid substance use disorders. By far, however, the major source of early mortality is a very high risk of suicide (Angst et al., 1998; Tondo and Baldessarini, 2005; Tondo et al., 2003; Harris and Barraclough, 1997), with most studies indicating that when substance use disorders co-occur, the risk for suicidal behaviors increases (Comtois, Russo, Roy-Byrne, et al., 2004; Dalton, Cate-Carter, Mundo, et al., 2003). People with bipolar disorder tend to kill themselves while depressed or in a mixed state, as opposed to during periods of mania (Hawton, Sutton, Haw, et al., 2005; Institute of Medicine, 2002).

The Substances of Abuse

Substance use has generally been found to increase the likelihood of a suicide attempt, but the specific association between the different types of substances of abuse (with the exception of alcohol) and suicidal behaviour has not been clearly established (Borges et al., 2000). In many cases of suicidal behaviour abuse of drugs and alcohol are co-occurring, which makes it difficult to distinguish the contributions of each separately

(Harris and Barraclough, 1997). Research discussing the role of alcohol in elevating suicide risk is considerably more extensive and robust than similar research on the role of other drugs of abuse in suicidal behaviour. Felts, Chenier and Barnes (1992), in their study on adolescents in North Carolina, found that the use of cocaine/crack was more closely associated with a self- reported incidence of attempted suicide than was the use of alcohol, marijuana or needle drugs.

Analysis of data on 7,227 suicides in 2003 (Serpi et al., 2005) indicated that among suicide victims who tested positive for substances, 33.3 percent tested positive for alcohol, 16.4 percent for opiates, 9.4 percent for cocaine, 7.7 percent for marijuana and 3.9 percent for amphetamines.

Anxiety Disorders

Anxiety disorders are common psychiatric illnesses that can result in considerable functional impairment and distress (Hollander and Simeon, 2003). In treating patients with anxiety disorders, suicide risk is often not in the forefront of the clinician's mind as it can be for conditions such as major depression, bipolar disorder, substance abuse, personality disorders, and schizophrenia. However, a minority of anxiety disorder patients develop serious suicidal ideation and even make suicide attempts, sometimes successfully (Oquendo et al., 2005; Zimmerman and Chelminski, 2003; Hollander et al., 1997; Schneier et al., 1992; Allgulander and Lavori, 1991).

In a sample of 327 psychiatric out-patients in Iowa City, USA (Naragon-Gainey and Watson, 2010) Post-traumatic stress disorder (PTSD) resulted to be significantly related to suicidal ideation also after controlling for co-morbidity, while associations with the other anxiety disorders all dropped to non-significance. This finding is consistent with previous research (e.g. Marshall et al., 2001; Oquendo et al., 2003; Sareen et al., 2005).

Panic Disorder

The association between panic disorder (PD) and increased suicide risk was first identified more than two decades ago. Allgulander and Lavori (1991) conducted a large retrospective survey in Sweden and found an increased suicide risk in PD in the absence of comorbid diagnoses.

U.S. epidemiologic data initially appeared to support this finding, because the original

Epidemiologic Catchment Area (ECA) study analyses reported a 47% rate of suicidal ideation and a 20% rate of suicide attempts in adults with a lifetime diagnosis of PD (Weissman et al., 1989). Subsequently, the same data were reanalyzed to account for comorbidity, and it was determined that PD patients with major depression had a 19.5% rate of suicide attempts in contrast with a much lower 7% in uncomplicated panic. Still, this lower rate was higher than that encountered in the general population and was comparable with the 8% rate in uncomplicated major depression (Johnson et al., 1990). Further reanalysis of the ECA data, after controlling for all comorbidity rather than one disorder at a time, could no longer show an association between panic and suicide attempts (Hornig and McNally,1995). A recent report established that lifetime PD, in the presence of other disorders, was unrelated to elevated risk of suicide attempt and did not account for additional variance; participants with PD alone were also not at increased suicide attempt risk (Vickers and McNally, 2004). Clinical samples have revealed similar patterns and inconsistencies (Lepine et al., 1993). In two different samples of outpatients with PD several predictors of suicidality were identified: Cluster B and Cluster C personality, history of substance abuse and comorbid depression (Ozkan and Altindag, 2005; Warshaw et al., 2000; Starcevic et al., 1999; Friedman et al., 1999).

All studies taken together then suggest that, for the most part, suicide attempts in panic disorder are strongly associated with mood disorder, personality disorder, and substance use comorbidity. Suicidal ideation in the absence of attempts may be more specifically associated with the experience and impact of the panic disorder itself. The association between pure panic disorder and suicide attempts is still controversial.

Generalized Anxiety Disorder

Suicidality in GAD has not been well studied, and findings are often confounded by the presence of depression. In one large survey of GAD and major depression in a primary care setting, it was found that comorbid GAD and major depression were associated with higher suicidality than either diagnosis alone (Wittchen et al., 2002). In adolescents, GAD has been found to be associated with suicidal ideation but not with suicide attempts (Strauss et al., 2000). The recent Sequenced Treatment Alternatives to Relieve Depression (STAR*D) trial reported that patients with anxious major

depression are more likely to be suicidal than those with nonanxious depression, and they often have GAD comorbidity (Fava et al., 2004). As in the STAR*D trial, another study of 332 psychiatric outpatients with major depression found that those with comorbid GAD, even if occurring only in the context of the depressive episode, had poorer functioning and greater suicidal ideation, and GAD was more likely to be found in their first-degree relatives (Zimmerman and Chelminski, 2003).

Although we know little about suicidality in GAD, it appears that two major correlates of suicidality in GAD are comorbidity with major depression and deterioration in functioning.

Social Phobia

Schneier et al. (1992) examined the morbidity associated with social phobia (SP) in a large sample of 13,000 adults who participated in the ECA study. Suicidal ideation rate was significantly elevated in social phobia even after comorbidity was controlled for. The suicide attempt rate was significantly elevated only in the presence of comorbidity (15.7%) but was comparable to the rate in those without psychiatric illness in uncomplicated SP (0.9%). The latter finding of elevated suicide risk in SP in the presence of other psychiatric disorders has been corroborated by other studies (Nelson et al., 2000; Weissman et al., 1996). A clinical study of 41 adult patients with SP employed the five ECA suicide questions and reported a 12% rate of lifetime suicide attempts (Cox et al., 1994). The authors found attempts to be higher in women (21%) than in men (4.5%); women also had higher suicidal ideation (47%) than did men (23%). The patients who had made attempts were significantly more likely to report that they had received past treatment for depression and that they had been psychiatrically hospitalized, whereas those who experienced suicidal ideation had higher depression scores.

Two twin community studies have both identified SP as a major psychiatric correlate of suicide attempts (Glowinski et al., 2001; Statham et al., 1998). Statham et al. (1998) examined lifetime prevalence of suicidal thoughts and behavior in a large community-based sample of monozygotic and dizygotic twin pairs. With respect to psychiatric disorders, it was found that history of SP was strongly associated with suicide attempts in women (odds ratio=15.6) but not in men. When all psychiatric disorders were

examined together, major depression was the strongest predictor of suicidality, yet SP remained a significant predictor.

It therefore seems that SP -both on its own and in the presence of comorbidity, especially depression- bears an elevated suicide attempt risk, possibly more so in women.

Obsessive-Compulsive Disorder

Suicidal ideation and suicide attempts may be more common in OCD than one might expect. A large survey of 701 OCD patients, although subjective in nature, revealed that over half of the sample had thought about suicide and about one-eighth had actually attempted suicide secondary to their obsessive-compulsive symptoms (Hollander et al., 1997).

Although the precipitants of suicide attempts were not specifically stated in this report, suicidality appeared related to the large toll that the disorder can take on psychosocial functioning. Compromised functioning was widely endorsed by survey participants, who frequently reported probable or definite OCD interference with their career aspirations (66%), marital relationships (64%), academic achievements (60%), loss of intimate relationships (43%), and loss of work (22%). On the other hand, in a clinic-based sample of 1,979 children and adolescents, elevated suicidality was not found for OCD (Strauss et al., 2000). Even adolescent inpatients with OCD have been reported to have very low rates of suicide attempt histories (Apter et al., 2003). It seems reasonable to hypothesize that OCD usually takes a more chronic and gradual toll, with steady deterioration in relationships and vocation that can occur over many years and eventually lead to suicidality.

Post-traumatic Stress Disorder

Suicidal ideation and suicidal attempts are well known to occur in the context of PTSD. In a national sample of women who had been sexually assaulted during childhood or adulthood, a significantly greater likelihood of suicide attempts was identified, controlling for demographic factors and other psychosocial characteristics (Ullman and Brecklin, 2002). Clinical samples concur on the marked prevalence of suicidality in PTSD patients. In male veterans, suicidal thoughts were reported in 70% and suicide

attempts in up to 25% (Butterfield et al., 2005). In chronic civilian PTSD, suicidal ideation was reported in 38% and suicide attempts in 10% of the sample (Tarrier and Gregg, 2004). Even adolescent (Mazza, 2000) and childhood (De Bellis et al., 1999) PTSD has been associated with greater suicidality.

Several studies have examined the impact of comorbidity and trauma history on the relationship between PTSD and suicidality. Oquendo et al. (2005) reported that in a sample of 230 patients with major depression, of whom about one-quarter had comorbid PTSD, PTSD comorbidity was significantly associated with suicide attempt history. The PTSD comorbid group had greater severity of depression, impulsivity, and hostility; more Cluster B personality disorder comorbidity; and greater childhood abuse histories. Of all predictors, Cluster B personality disorder was the only independent variable related to lifetime suicide attempts.

In a sample of patients with chronic civilian PTSD, suicidal behavior was associated with impaired functioning, depression, and prescribed psychotropic medications (Tarrier and Gregg, 2004). In a national sample of sexually assaulted women, number of lifetime traumatic events and depression were each associated with the likelihood of suicide attempts (Ullman and Breckin, 2002). In a female sample of physical partner abuse, PTSD was found to mediate the relationship between the abuse and suicide attempts (Thompson et al., 1999). In a comparison of subjects with PTSD, other anxiety disorders, and normal volunteers, patients with PTSD were found to have the greatest suicide risk; impulsivity increased the risk, whereas social support mitigated it (Kotler et al., 2001).

In a study of 106 adolescents in an urban high school, controlling for depression and gender, PTSD symptoms were significantly associated with suicidal ideation and marginally associated with attempts; severity of PTSD also was associated with suicidality (Mazza, 2000).

In summary, PTSD may be more clearly associated with suicidality than any other anxiety disorder. Factors associated with such suicidality are depression, Cluster B personality traits, greater childhood and lifetime trauma, severity of PTSD symptoms, and poor social supports.

In contrast to other psychiatric illnesses such as mood, psychotic, substance use, and personality disorders, there are more discrepancies, uncertainties, and limitations in the available data regarding suicidality in the anxiety disorders (Khan et al. 2002). There are several possible explanations for this, such as the common impression that suicidality is not as much of an issue in anxiety disorders, accuracy of diagnostic and suicidality assessment and types of samples studied, and reliability in the diagnosis of comorbid disorders. A recent meta-analysis of the U.S. Food and Drug Administration database of 20,076 patients participating in anxiety disorder treatment trials revealed an annual completed suicide risk rate of 1.93/1,000 and an annual suicide attempt risk of 13.5/1,000 (Khan et al. 2002). These estimates are possibly conservative given all the restrictions of clinical trials and highlight that suicidality may be higher in anxiety patients than previously thought.

Schizophrenia

The management of suicidality in patients with schizophrenia represents a common but highly challenging problem for clinicians. The lifetime prevalence of completed suicides and suicide attempts in this patient group is much higher than in the general population, with a generally accepted range of 5%-10% for completed suicides and 25%-50% for suicide attempts (Palmer et al. 2005). The basics of the proper assessment and management of the suicidal patient with schizophrenia share many features with the treatment of suicidality in other patient populations. For example, factors such as previous attempts, comorbid depression or substance abuse, and male gender confer higher suicide risk in individuals with schizophrenia, mirroring important risk factors in the general population.

A small study of 50 patients hospitalized for schizophrenia found that 36 percent of the patients also abused substances (Gut-Fayand et al., 2001). (Other studies have found higher rates of substance use disorders in this population.) Of these, 78 percent had attempted suicide at least once, compared with 42 percent of patients with schizophrenia who did not abuse substances.

Most are in a depressive rather than a psychotic state when they die, and more than half made previous serious attempts.

Eating Disorders

Multiple studies find high rates of suicide in patients with anorexia nervosa (Standardized Mortality Ratio for suicide range from 1.0 to 5.30, whereas suicide rates do not appear to be elevated in bulimia nervosa. In contrast, suicide attempts occur in approximately 3–20% of patients with anorexia nervosa and in 25-35% of patients with bulimia nervosa. Clinical correlates of suicidality in eating disorders include purging behaviors, depression, substance abuse, and a history of childhood physical and/or sexual abuse. Patients with eating disorders, particularly those with comorbid disorders, should be assessed routinely for suicidal ideation, regardless of the severity of eating disorder or depressive symptoms (Franko and Kell, 2006).

Personality Disorders

Personality disorders (PDs) are associated with estimated lifetime rates of suicide ranging from 3% to 9% (American Psychiatric Association, 2003). Compared with the general population, the estimated risk for suicide is about 7 times greater in persons with personality disorder (Harris and Barraclough, 1997) and about 13-fold for formerly hospitalized patients with PDS (Zilber et al., 1989; Black and Winokur, 1986). From a different vantage point, psychological autopsy studies have shown that about 30% of those who die by suicide had at least one personality disorder (Isometsa et al., 1996; Lesage et al., 1994). The prevalence of PDs among adolescent and young adult suicide completers has been reported to be even higher, with nearly half having a personality disorder (Linehan et al., 2005; Brent et al., 1994; Lesage et al., 1994; Apter et al., 1993). Similarly, among psychiatric outpatients, half of patients who die by suicide had a personality disorder (Brown et al., 2000; Baxter and Appleby, 1999).

This estimation varies depending on the type of personality disorder (Cluster A, B, or C or individual disorders) or on the presence of comorbidities, especially mood and substance use disorders. Of note, self-injurious behavior is an important risk factor for suicidal behavior, because 55%-85% of patients with self-injurious behavior have made at least one suicide attempt (Stanley and Brodsky, 2005). Suicidality is a criterion for the diagnosis of borderline personality disorder (BPD; American Psychiatric Association, 2000). Among individuals treated for borderline personality disorder, the majority report a previous suicide attempt (Davis, Gunderson, Myers, 1999; Linehan et

al., 2000). This is particularly true for young adults, who are more likely to be diagnosed with these disorders than their older counterparts. Solid epidemiological data are unavailable but it has been estimated that suicide may occur at a lifetime rate of about 9 percent among those with BPD (Davis et al., 1999). A large-scale study of alcohol-dependent inpatients that rigorously assessed all of the personality disorders defined by the Diagnostic and Statistical Manual, Third Edition, Revised showed that BPD alone was associated with a lifetime suicide attempt, after controlling for other risk factors and personality disorders (Preuss, Koller, Barnow, et al., 2006). The relevance of this study to suicide deaths is unclear.

Impulsiveness, and Impulsive Aggression

A longstanding hypothesis is that impulsive aggression (also commonly referred to as reactive aggression) is a potent risk factor for suicidal behavior (Conner, Duberstein, Conwell, et al., 2003; Turecki, 2005). Individuals prone to this type of aggression experience emotional hyperarousal including anger and anxiety, have poor modulation of physiological arousal, and show a loss of behavioral control (Barratt, 1991), characteristics that are presumed to describe an acutely suicidal state (Shneidman, 1985). An empirical review of studies of personality measures and suicide showed an association between suicide and continuous trait measures of aggression and impulsivity (Conner, Duberstein, Conwell, et al., 2001). Most measures appeared to tap constructs most relevant for impulsive aggression: impulsivity (Duberstein, Conwell, Caine, 1994), anger (Angst and Clayton, 1998), explosiveness (Farberow, Kang, Bullman, 1990), irritability (Allebeck, Allgulander and Fisher, 1988; Berglund, 1984), and reactive aggression (Angst and Clayton, 1998). Similar findings have been reported in studies of suicide attempts. For example, an influential study that showed that a measure of "aggression/impulsivity," created by combining scales of aggression and impulsiveness, was a potent correlate of suicide attempts in a high-risk clinical sample (Mann et al., 1999). These reports and other studies of aggression, impulsiveness, and related scales in suicide and attempted suicide are summarized in a recent review (Brezo, Paris and Turecki, 2006).

SUICIDALITY IN THE PERINATAL PERIOD

Perinatal Psychiatry

'Perinatal psychiatry' is now the internationally accepted term for conditions complicating pregnancy and the postpartum year. These include not only new-onset conditions following delivery such as postnatal depression and puerperal psychosis, but also pre-existing conditions which may relapse, recur or continue during pregnancy and the postpartum period (Austin, 2010).

It is concerned not only with the medical and psychosocial management of the mother but also the impact of the disorder and its treatments on the developing infant before and after birth. Although in Italy perinatal psychiatry is a sub-specialty of adult psychiatry, it overlaps and shares common goals with child psychiatry and those concerned with infant development.

Although there has been prominent research interest in perinatal psychiatric disorders for over 40 years with individual centres of excellence for the provision of care, in general, services have been patchy, inequitable and at a national level, inadequate. Only recently has this been recognised and a number of national policies and practice guidelines issued to rectify the problem (Royal College of Psychiatrists, 2000; Lewis & Drife, 2001; Scottish Executive, 2001; Department of Health, 2002; Scottish Intercollegiate Guidelines Network, 2002; Department of Health, 2004; Lewis & Drife, 2004; Lewis, 2007; National Institute for Health and Clinical Excellence, 2007).

Pregnancy and childbirth is associated with a considerable psychiatric morbidity. A small but significant number of women will develop a profound psychotic illness in the early weeks following childbirth requiring specialist skills and resources for their and their infant's proper care. Although the number is small, it represents a substantial increase in risk of developing a psychotic illness following childbirth compared with other times. A larger number of women will develop a severe non-psychotic affective disorder and an even lager number mild to moderate affective disorder popularly known as postnatal depression.

Overall, at least 10% of delivered women will experience a psychiatric disorder following childbirth. The more severe conditions, such as those cases complicated by

suicidal ideation and / or suicide attempts, will require the attention of specialised mental health services. The less severe conditions, although probably no more common than at other times, pose a major public health problem, with chronic maternal depression, particularly if associated with socio-economic adversity, having adverse effects on infant and child development.

The perinatal period is also very important because of the risk of recurrence in women with pre-existing serious mental illness, particularly bipolar disorder. Childbirth is unique in psychiatry as a major provoker of mental illness that comes with 9 months warning.

The perinatal period poses particular problems for the management of psychiatric disorders: many psychotropic medications, particularly mood stabilisers, are problematic in pregnancy; acute psychotic episodes in pregnancy compromise maternal and infant health. The distinctive clinical presentation, rapid onset and deterioration can demand a different response from psychiatric services than at other times. Throughout the perinatal period psychiatric professionals have to deal with two patients, both mother and infant. All of these factors consistently revealed by research over the years have been reinforced by the findings of the last four maternal deaths enquiries in the UK (Department of Health, 1998; Lewis & Drife, 2001, 2004; Lewis, 2007).

Pregnancy and the early postpartum period is exceptional for its level of surveillance by health professionals. This provides an opportunity not only for the early detection and prompt treatment of women who are ill but also for the identification in early pregnancy of those at risk of developing an illness following delivery and for secondary and perhaps primary prevention.

Most of the UK national policies for perinatal mental health have been strongly influenced by the UK maternal mortality enquiries over the past 4 years. These reveal that suicide in particular and psychiatric causes of maternal deaths in general are a leading cause of maternal mortality. This is also likely to be true internationally. It is generally accepted that maternal mortality is the ‘tip of the iceberg’ and it is therefore reasonable to assume that psychiatric disorder is also a leading cause of maternal morbidity.

In its current form, the Confidential Enquiry into Maternal Deaths (CEMD) is over 50

years old. In the UK, suicide has always been included as an indirect cause of maternal death; however, it is only since 1994 that suicide and other psychiatric causes of maternal death has been separately analysed and presented in the written report and a psychiatrist has been appointed as one of the central assessors to the CEMD.

The CEMD combines both a maternal mortality surveillance and quantitative data analysis with an enquiry into individual cases revealing a description of the pathways of care and circumstances that were associated with an individual death. This combination of methods allows for the identification of themes and factors associated with poor outcome that in its turn has led to the development of practice guidelines with demonstrable impact on the quality of maternità care. In addition, it allows for the emergence of new themes which reflect not only changes in reproductive epidemiology and technology (e.g. increasing maternal age, rise in Caesarean sections, *in vitro* fertilisation) but also rapid societal changes such as the impact of asylum seekers and immigrants.

Classification of Maternal Deaths

"Maternal deaths" were traditionally defined as occurring any time during pregnancy and up to 42 days postpartum, with additional classification as "direct", "indirect" or "incidental"(WHO, 1993). Direct deaths result from obstetric complications (eg, eclampsia). Indirect deaths result from a condition that is not directly related to obstetric causes but is aggravated by the effects of pregnancy (eg, a cardiac condition) (WHO, 1993).

More recently, the classification of maternal deaths was broadened (ICD-10 coding) to include late maternal deaths, that is, deaths from direct or indirect causes between 43 and 365 days postpartum (WHO, 1993)

Deaths associated with psychiatric illness are increasingly being included in the category of late maternal deaths. It is well recognised that maternal deaths due to psychiatric illness have been under-reported, partly because of misclassification of suicides as incidental deaths, and partly because of under-reporting of late maternal deaths (Hoj et al., 2003). Late maternal deaths are more difficult to identify, as they often occur after women have ceased to attend maternity services.

Researching deaths thereafter is reliant on various data collections (including coroners' reports and state registries of births, deaths and marriages), which in the past have not necessarily identified death in relation to giving birth, thus making them a less reliable source of information. In Australia, this problem is now being addressed by the inclusion of an item on death certificates enquiring about pregnancy in the preceding year and the incorporation of ICD-10 coding into coroners' reports.

Actually, before 1997 in Australia deaths from psychiatric illness, apart from puerperal psychosis (which was classified as a direct cause), were classified as incidental maternal deaths (conditions occurring during pregnancy but for which the pregnancy is unlikely to have contributed significantly to the death).

In line with recommendations from the 1997-1999 Confidential Enquiries into Maternal Deaths in the United Kingdom (the "National Institute for Clinical Excellence [NICE] report") (CEMD, 2002), Australia has classified these deaths as indirect since the 1997-1999 triennium.

Since 1997, case ascertainment has been enhanced by an Office of National Statistics Linkage Study which identifies maternal deaths not reported directly to the CEMD. These deaths have been in the majority late indirect and coincidental deaths but have included a substantial number of suicides. Until the 2003-2005 CEMD, suicide was the second leading cause of indirect death (pregnancy and up to 42 days after delivery of the infant) but the leading cause of maternal death overall (up to 1 year) (Lewis and Drife, 2001, 2004). In the latest CEMD (2003-2005; Lewis, 2007), there has been a significant reduction in the numbers of suicides so that suicide is now the third leading cause of indirect deaths and the second leading cause of maternal death up to 1 year. Despite this reduction, a number of features of maternal suicide have remained constant over the last three CEMDs, reflected in the recommendations of the enquiry and its implications for both psychiatric and maternity practice.

Maternal Suicidality

'Why Mothers Die 2000-2002' (Lewis and Drife, 2004), highlighted suicide as a major cause of maternal death, and, like the 1997-1999 CEMD report (Lewis and Drife, 2001), found suicide to be the leading cause of indirect or late-indirect deaths for the year following delivery.

Lindahl et al. (2005) estimate that suicide accounts for 20% of maternal deaths even though the rate for all delivered women in the year after birth is lower than that of the general population.

Despite high rates of psychiatric morbidity during childbearing years, including elevated levels of depression as well as postpartum depression and psychosis (Oates, 2003; Nonacs and Cohen, 2003; Sloan and Kornstein, 2003), studies have found a low risk of fatal self-harm in childbearing women.

'Saving Mothers' Lives' (Lewis, 2007) found a decrease in the numbers of maternal suicide, which if it persists in the next triennium, will suggest that some of the strategies recommended are being implemented.

The suicide rates for women during pregnancy and up to 2 years postpartum are fractions of those expected after adjustment for age (Appleby, 1996; Oates, 2003). In one Canadian study (Turner et al., 2002), only 0.02% of maternal deaths resulted from suicide in the period between 20 weeks of gestation and 42 days postpartum.

In the period of 43 days to 225 days postpartum, 0.5%-1.0% of deaths were due to suicide. The researchers concluded, "Although postpartum depression clearly affects many women, it apparently does not result in an increased incidence of suicide" (Turner et al., 2002, p. 35).

Notably, the risk of suicide associated with severe psychiatric illness, particularly psychosis, appears to outweigh the protection conferred by pregnancy and childbirth; although postnatal women in general may have a low rate of suicide, those who develop severe postpartum illness are at high risk, particularly during the first year after childbirth (Appleby et al., 1998). In one study in which suicide was the leading cause of all maternal deaths either during pregnancy or up to 1 year postdelivery, 85% of the women had identified psychiatric problems and were receiving treatment. At least 68% were psychotic or had severe depressive illness (Oates, 2003). In another study,

suicides that did occur were committed by psychotic women (Appleby, 1996).
One group of researchers found that the overall risk of suicide in women admitted to psychiatric hospitals in the year following childbirth increased 70-fold.
This figure was consistent with the elevated suicide rates found within the first year of discharge of individuals hospitalized for psychosis (Appleby et al., 1998) and in particular in the first week after discharge (Qin and Nordentoft, 2005).

The overwhelming majority (over foreword 80%) of maternal suicides had a previous psychiatric history. In the 1997-2002 CEMDs (Lewis & Drife, 2001, 2004), 50% of maternal suicides had a previous history of serious mental illness, contact with psychiatric services or admission to a psychiatric unit. In the main, women had either bipolar disorder or puerperal psychosis. These identifiable risk factors had not been detected in early pregnancy nor had proactive management plans been put in place. The postpartum recurrence seemed to have taken all by surprise and there was a delayed response to the women's rapidly deteriorating illness.
The majority of these women died within the first 3 months following childbirth. None had been admitted to a mother and baby unit or cared for by specialised perinatal psychiatric services in either their current or previous maternities.
In the latest CEMD (Lewis, 2007), a smaller proportion (37%) of maternal suicides had these characteristics. The reduction in maternal suicides was accounted for by a reduction in the number of women who died in late pregnancy or within the first 3 months postpartum. However, the majority of women who died from suicide within 3 months of delivery had the same characteristics as previously reported, that is to say a **past history of serious mental illness**, **a failure to identify and manage their risk**, a serious and **rapidly deteriorating postpartum illness and a lack of management by specialised services**.

Suicide is not the only psychiatric cause of maternal death. A worrying theme to emerge from the last CEMD was the overall significant contribution of **substance misuse** to maternal mortality. Of all maternal deaths, 10% occurred in substance misusers, 57% of psychiatric deaths.
Substance misuse was associated with avoiding antenatal care, high rates of removal of

the infant into the care of local authorities and the subsequent modern management of perinatal psychiatric disorder absence of both psychiatric and maternity care for the mother. Very few of these women had had specialist care from drug addiction services during their pregnancies and this led to additional recommendations from the last CEMD.

A review in 1968 estimated that between 5 and 12% of women attempting suicide were pregnant (Whitlock and Edwards, 1968). In 1984, 0.07% of calls to a US metropolitan poison control centre were from or about pregnant women (Rayburn et al., 1984) and the attempt reported was usually her first. Half of the overdoses reported were taken during the first trimester, most commonly using an over-the-counter analgesic, iron or a vitamin.

One review assessed 27 studies that reported rates of suicidal ideation, intention, attempts and completed suicide in pregnant and postpartum women (Lindahl et al., 2005). Suicidal thoughts (assessed by endorsement of item 10 on the EPDS, 'the thought of harming myself has occurred to me') occurred in up to 14% of pregnant women.

The authors observed lower rates of suicide during pregnancy than that in the general population, but that when suicide did occur, violent methods were used.

Particular groups at risk are teenagers and women from cultures where being unmarried and pregnant is stigmatised. Women with past histories of abuse are also more likely to die by suicide. A US study of over 2000 women who attempted suicide found that those more likely to harm themselves were young, single, multiparous, less well-educated and more likely to be African-American. Of these, 26% misused substances (Gandhi et al, 2006). Follow-up found that those who self-harmed were more likely than controls to have a preterm labour, a Caesarean delivery and require a blood transfusion. Their infants showed an increased risk of respiratory distress syndrome and low birth weight.

Infanticide-neonaticide

Although the majority of women who die by suicide do not also kill their infant, the 2000-2002 CEMD report (Lewis and Drife, 2004) identified three cases where the

infant was also killed at the time of the suicide. In two cases, an older child was also killed at the same time and four suicides occurring in pregnancy near term also resulted in the death of a viable infant. Infanticidal ideas are common in populations with severe postpartum mental illness.

Chandra et al. (2002) report 43% having suicidal ideas, 36% reporting infanticidal behaviour and 34% reporting both.

Depression and psychotic puerperal psychosis ideas predicted infanticidal ideas, while the presence of psychotic ideas towards the infant predicted infanticidal behaviour.

Infanticide is a legal term used in the UK to refer to the killing of a child under the age of 12 months; **neonaticide** is not a legal term but refers to the killing of a child within 24 h of birth. Craig (2004) has reviewed the associated factors and Friedman et al. (2005a) included infanticide and neonaticide in a wider review of child murder.

Women who commit neonaticide are usually young, poorly educated and primiparous. They are often living at home with their parents and often have concealed their pregnancy. Most do not have a mental illness at the time of killing their child. Very few of them have a psychotic disorder and where a psychiatric diagnosis is found, this is more likely to be a personality disorder or a mild or borderline learning disability.

Mothers who commit infanticide are more likely to be older and married or living with a partner. There is more likely to be a mental illness present and the infant death is often part of an extended suicide or occasionally an altruistic act based upon a delusional idea that some terrible fate was about to befall the infant. Mothers with schizophrenia who relapse in relation to pregnancy or childbirth may incorporate the infant into their delusional system or be acutely disturbed and carry out the act with no rational reason.

Substance misuse is a factor often associated with infanticide and only very rarely is it the consequence of factitious disorder by proxy.

Friedman et al (2005b) examined a case series of mothers who had killed their children and were adjudicated as ‘not guilty by reason of insanity’ (n=9). Their children’s ages ranged from birth to 16 years (mean=3.7; a third were infants). Over 80% of the mothers had a psychotic disorder or mood disorder with psychotic features and many had had recent contact with psychiatric services. Almost half had made previous suicide attempts and 56% had planned suicide along with the death of their child. Half

of these women had depression and the majority were experiencing auditore hallucinations including command hallucinations to kill their children.

Three-quarters were delusional at the time of the killing and two-thirds of these had delusions that involved their children. These delusions frequently involved a belief that the child was possessed by the devil or demons, that the mother herself was a god or religious figure and that some terrible thing would happen to the child. Over a third were pregnant or within the first postpartum year. The most common method used was suffocation.

A mother tends to kill only her children and herself. In contrast, a father who kills his children is more likely to kill his entire family, includine his spouse (Malphurs and Cohen, 2002; Nock and Marzuk, 1999). Among mothers who commit infanticide, 62% commit suicide (Attia et al., 1999; Brockington, 1996). In one study of suicide during pregnancy and the postpartum period, 5% of the suicides also committed infanticide (Appleby, 1996). One author has estimated that two-thirds of mothers who kill their children attempt suicide. These women are generally motivated from the wish to spare the children from some external impending harm or from enduring the pain of being motherless after the mother commits suicide (Brockington, 1996).

Suicidality During Pregnancy

Relative to suicide rates in the general female population, one study found women were less likely to screen positive for suicidal ideation during pregnancy (Stallones et al., 2007). Suicide attempt rates, as assessed by hospitalizations for intentional injuries, also resulted lower during pregnancy.

Suicidal ideation in pregnancy was a strong predictor of postpartum depression (Chaurdon et al., 2001) and pregnant women with depressive disorders are less likely than non-pregnant women to receive treatment (Vesga-Lopex et al., 2008).

Among the pregnant women who die by suicide, teenagers were reported to be at greater risk (Appleby, 1991).

Around the world suicide rates vary widely also according to different culture aspects: for example, women in nations that stigmatize motherhood among unmarried women, such as rural Bangladesh, tend to be at higher risk of suicide (Fauveau and Blanchet, 1989); Rizzi et al. (1998) reported on violent pregnancy deaths in the province of Cordoba –Argentina from 1992-1996- where abortion is illegal.

Increased social support, concern for the unborn child, and more contact with health care providers may work together to reduce the risk of suicide.

When suicide does occur, the use of violent methods of suicide among pregnant women suggests high levels of intent and may be related to higher levels of psychopathology in these women.

In an economically and racially diverse sample of pregnant women attending a university-based clinic, the prevalence of antenatal suicidal ideation was 2.7% (Kessler et al., 2005).

In the largest community-based study of the prevalence and correlates of antenatal suicidal ideation among pregnant woman, the prevalence of suicidal ideation was similar to that in nationally representative samples of non pregnants adults (Gavin et al., 2011); in other words, pregnancy was not a protective factor against suicidal ideation.

Gavin et al. (2011) have shown that antenatal major depression and psychosocial stress are significantly associated with antenatal suicidal ideation.

Suicidality in the Postpartum Period

A postpartum suicide attempt is a tragic event that may have serious long-term repercussions for the postpartum woman's family and her infant.

A recent study noted that a postpartum suicide attemp occurs in about 1 in 2277 live births in Washington State (Schiff and Grossman, 2006).

Prevoius studies of maternal mortality have reported that postpartum suicide rates range from 0.5 to 5.9 per 100000 live births (Gissler et al., 1996; Kleiner and Geston, 1984) and that suicide accounts for between 2.7% and 15% of all deaths to women within 1 year postpartum (Horon and Cheng, 2001; Jocums et al., 1998; Hogberg et al., 1994). In comparison, the suicide rate in the US female population for 2001 was 4.1 per 100000 (Anderson et al., 2001).

Women in the postpartum period can experience several **affective, anxiety, and psychotic disorders**, ranging in severity from the common "postpartum blues" experienced by 50-85% of mothers to postpartum psychosis with a prevalence of 0.2% among childbearing women (Clay and Seehusen, 2004). Appleby and Turnbull (1995) found that Danish women admitted to an inpatient psychiatric facility postpartum had a 70-fold increased risk of suicide in the year after birth and a 17-fold increased risk of suicide long-term compared with women in the general Danish population.

Kessler et al. (1999) reported that among the maternal deaths by suicide in the United Kingdom from 1997-1999, a significant proportion of the women had a psychiatric disorder.

A positive **depression** screen and previous suicide attempts are predictors of risk of suicidality (Pinheiro et al., 2008). In a population-based case-control study conducted in Washington, Comptois et al. (2008) found a significantly increased risk of postpartum suicide attempts among women with a psychiatric disorder or substance use or a dual diagnosis during prior hospitalizations.

Women with more than 1 prior **hospitalization** with psychiatric or substance use diagnosis were at a marked increased risk; women with 2 or more hospitalizations were at increased risk of postpartum suicide attempt compared with women with only 1 prior hospitalization similar to findings in a prior study of completed suicide in the general population (Gissler et al., 1996; Qin and Nordentoft, 2005). Multiple prior

hospitalizations may be a surrogate measure for a more severe or persistent disorder that is associated with increased risk.

Few studies have evaluated the **obstetric and perinatal risk factors** that are associated with suicide and suicide attempts among women who recently delivered a child. Gissler et al. (1996) found that among postpartum women, those who were **young** and **unmarried** and had **low socioeconomic status** were at increased risk for postpartum suicide compared with older, married women of higher socioeconomic status. Several studies have suggested that certain pregnancy outcomes also may be risk factors, with higher rates of postpartum suicide among women who had a **stillborn** (Appleby, 1991) or a **spontaneous or therapeutic abortion** compared with women who had a live birth (Shiff and Grossman, 2006; Gissler et al, 1996; Lester and Beck, 1988). Appleby (1991) noted a sixfold increased risk for postpartum suicide associated with fetal death. Case-control studies have demonstrated an association between suicide and suicide attempts (Benjaminsen et al, 1990; Agerbo, 2005; Qin and Mortensen, 2003) and sudden, intense, adverse personal experiences or losses such as the death of a close friend or relative, especially deaths from suicide.

Women who made postpartum suicide attempts used several different **methods.** The vast majority used medications for poisoning (88.7%), followed by cutting themselves (6.1%), hanging (0.3%), handgun (0.3%), extreme cold (0.3%), or crashed motor vehicle (0.3%). The method was unspecified in the hospital record in 4.0% (Comtois et al., 2008). Schiff and Grossman (2006) found that the majority of suicide attempts were poisonings; this figure is similar to a previous study by Appleby and Turnbull (1995) among postpartum women, as well as other studies in the nonpregnant female population (Miller et al., 2004; Murphy, 1998; CDC's, 2002). The use of tranquilizers or psychotropic medications indicates that case women may have had previous psychiatric morbidity.

Appleby (1991) noted an increase in the number of completed suicides in the first and the fifth months postpartum, whereas Schiff and Grossman (2006) found that suicide attempts were most frequent in the first and 12th months postpartum.

Suicidality and the mother-infant relationship

Relationships between depressed mothers and their infants are often characterized by impairments in the process of mutual regulation (Weinberg and Tronick, 1998). Cognitive and affective processes associated with postpartum depression, such as preoccupation, low maternal self-esteem, and **suicidal ideation**, can manifest in many ways in the mother-infant relationship. For example, mothers can be disengaged from infants, talk less, show fewer facial expressions, share less of their attention to an object, and touch their infants less frequently (Field et al., 2007; Weinberg et al., 2001). Chronic disruptions of the mutual regulatory interchange between mothers and infants strain attachment processes, impair infant social-relational learning and development, and interfere with the infant's ability to regulate his or her physiological, affective, and interactional states (Brockington, 2004; Teti, 2000; Sokolowski et al., 2007).

Infants of depressed mothers can show fewer affectively positive facial expressions and vocalization, more withdrawal, less attentiveness to the mother, decreased activity level, greater fussiness, and overall less engagementwith people and objects (Field, 2008; Feldman et al., 2009; Weinberg and Tronick, 1998).

In the long term, the quality of the early mother-infant relationship appears to predict aspects of child development, such as diverse forms of psychopathology, behavioral problems, and disruptions in cognitive abilities (Feldman and Eidelman, 2009; Lyons-Ruth, 2008; Milgrom et al., 2004; Righetti-Veltema et al., 2003).

Given that postpartum depression (PPD) was estimated recently to occur in as many as 19% of new mothers (Gavin et al., 2005), and that suicidal ideation is thought to be a common aspect of PPD, it is imperative to understand more about the population of women struggling with these problems and to study the impact of suicidality on parenting and the mother-infant relationship.

Suicidal ideation when co-occurring with postpartum depression shares many of the same symptoms, yet there are additional experiential aspects that can be detrimental to the mother and her relationship with her infant.

People who are suicidal can cognitively distort a small stressor into a lethal one (Shea, 2002). An overwhelming external stressor such as a pregnancy or the birth of a baby can precipitate feelings of hopelessness and trigger thoughts of self harm (Pollock and Williams, 1998). Many mothers with PPD experience shame and humiliation in

viewing themselves as the worst mothers in the world; they imagine that others see them this way as well. Such inner conflict can trigger suicidal thoughts for a woman who focuses on the ideas that her baby will be better off without her or that she may hurt her baby if she lives (Beck, 2002).

Additionally, suicidal people have demonstrated poor problem-solving abilities in the context of cognitive rigidity and an overall passive approach to dealing with life's challenges. When struggling with thoughts of self-harm they are unable to generate many alternative solutions to problems (Pollock and Williams, 2004).

These problem solving deficits appear independent of mood, so improvement in depressive symptoms for mothers with postpartum depression will not necessarily improve their ability to solve dilemmas they face with their infants.

Women who become depressed and suicidal in pregnancy or postpartum are unable to manage the stress of a new infant and have poor abilities to respond to the challenges of motherhood, specifically the day-to-day interactions with their baby. As described above, these interactions involve many instances of attunement and responsiveness depending on the needs of the infant.

Performing these tasks with reduced hours of sleep, low energy, and preoccupation with depressive internal states is a feat of grand proportions for mothers with PPD.

Although many manage to complete necessary caregiving tasks in a mechanical manner by accessing "maternal instincts" and empathy for their infant (Barr, 2006), those who are suicidal are further hampered by their compromised ability to develop appropriate responses to their infants' increasing demands (Noorlander et al., 2008).

Often they are passive in their approaches, demonstrating hopelessness in their interactions with infants. It is possible that the more the mother is unable to care for her infant the more depressed and suicidal she becomes. For some mothers with PPD suicidal ideation has become part of the postpartum experience (Beck and Indman, 2005).

A recent paper (Paris et al., 2009) has presented data collected prior to treatment from a mixed method research project evaluating the effectiveness of a home-based mother-infant psychotherapy.

The intervention, called **Early Connections**, is aimed at decreasing postpartum

depression and mitigating its impact on the mother-infant relationship (Spielman, 2002).

The study examined the relationship between suicidality and mother-infant interactions in a clinical sample of women with postpartum depression and a wide ranging levels of suicidal thinking

When divided into low and high suicidality groups, the mothers with high suicidality experienced greater mood disturbances, cognitive distortions, and severity of postpartum symptomotology: they were more depressed and anxious. The high suicidality group also scored significantly higher on the psychoticism and obsessive-compulsive subscales, indicating greater distortions in thinking and cognitions, was also more interpersonally sensitive and tended to experience more somatic symptoms. Furthermore, woman with high suicidality had lower maternal self-esteem, more negative perceptions of the mother-infant relationship, and greater parenting stress. In fact, the more suicidal mothers strongly perceived that they were less prepared for mothering and they expected a poorer relationship with their infants; they perceived overall perenting as significantly more dysfunctional and distressing than women lower in suicidality.

Observers rated highly suicidal mothers as significantly less able to demonstrate sensitivity and reciprocity with their infants during unstructured interactions. For example, these dyads demonstrated more problematic mutuality in that mothers were less aware of their babies' social signals and showed poorer ability to respond to them consistently. Additionally, mothers showed less positive affect and vocal appropriateness with their babies and focused their gaze less frequently on them.

The infants of the more suicidal mothers exhibited significantly less positive affect in the form of sounds or smiles and slightly more negative affect in the form of crying and fussing (marginal significance) in unstructured interactions. In addition, demonstrating the difficulties in the mutual regulatory process, babies initiated involvement with their highly suicidal mothers significantly less often in structured interactions and marginally so in unstructured ones. Infants of highly suicidal mothers were somewhat more passive and less engaged in the interactions.

Ultimately, as Cramer (1998) has posited, these findings demonstrate that postpartum

depression is a relationship disorder. Both mothers and infants are engaged in the process; mothers by being less sensitive and responsive, and infants by less involvement and positive affect and marginally more negative affect in interactions.
If the disorder is based in the relationship it makes sense to treat the mother-infant dyad in order to improve the mother's depression and suicidality as well as mother-infant interactions (Nylen et al., 2006). Many authors have suggested this approach for women with PPD, suicidal ideation or other difficulties that challenge attachment processes (Paris, Bolton, Weinberg, 2009; McDonough, 2004; Slade et al., 2005; Stern, 1995).

Hopefully, the DSM IV's omission of disorders involving the pathology of early parent-to-infant attachment will be corrected in DSM V. The construct of maternal and paternal sensitivity to their infant is now well understood, and its underlying dimensions have been defined (De Wolff and Ijzendoorn, 1997; Smith and Pederson, 1988; Pederson et al., 1998).

Parity and Risk of Suicide

Childbearing is considered to have long-term effects on women's health (Koski-Rahikkala et al., 2006). However, little is known about the relation between parity and mortality among women except for cancers of the reproductive organs (Green et al., 1988).

In his book on suicide published in 1897, Durkheim concluded that the rate of death from suicide was lower among married women than among unmarried women, because of the effect of parenthood and not marriage per se (Durkheim, 1966).

Three studies since then have explored Durkheim's hypothesis. Hoyer and Lund (1993) conducted a prospective study and reported a negative association between suicide-related mortality and number of children; in a nested case-control study in Denmark involving 6500 women who committed suicide, Qin and Mortensen (2003) found a significantly decreased risk of suicide with increasing number of children.

In the third study, 12055 pregnant women in Finland were followed up from delivery in 1966 until 2001: the authors found a decreasing trend in suicide-related mortality with increasing parity (Koski-Rahikkala et al., 2006).

Even in the prospective study involving 989949 women followed for 15 years, only 11 deaths from suicide occurred among women with six or more children (Hoyer and Lund, 1993). A more recent cohort study (Yang, 2010) found a 39% decrease in suicide-related mortality among women with two live births and a 60% decrease among women with three or more births compared with women with one child. The protective effect of parity on risk of death from suicide was much stronger than previously reported estimate (Hoyer and Lund, 1993; Qin and Mortensen, 2003).

Selection effects are likely to be an important explanation for this association. Psychiatric illness may affect opportunities for marriage and motherhood and decisions about subsequent childbearing (Hansen and Jakobsen, 1989; Kiernan, 1988; 1989; Howard et al., 2002). Women who are depressed are less likely to have stable relationships, probably because of the impact of the illness on their behaviour (McGrath et al., 1999). Research has shown that men become depressed when their

wives are depressed .(Burke, 2003) These factors may lead to a decreased desire to have a child or more children (Lapane et al., 1995; Stoleru et al., 1993).

The higher suicide rate among women with one child than among women with two or more children may be due in part to selection effect, because the group of women with one child will include those with problems, including ones related to first pregnancy, which prevented or discouraged them from having more children.

On the contrary, women in better health, physically and mentally, or who generally lead happier lives are more likely to have children (Qin and Mortensen, 2003).

It is difficult to explain whether the presence of children per se offers protection against suicide. Veevers (1973) suggested that the presence of children is protective against suicide only as long as they are cared for by their parents and that the protective effect disappears after the children leave

home.

The presence of young children may increase the mother's feelings of self-worth, possibly based on her perception of being needed (Qin and Mortensen, 2003). Consequently, the possibility was high that young children played a role in a woman's decision not to commit suicide.

Another explanation might be that children can provide emotional and material support to the mother when she has difficulties or setbacks (Qin and Mortensen, 2003). In addition, motherhood may enhance social networks, provide a positive social role and a potentially important source of social support, especially over the long term (Grundy and Shelton, 2001).

AIMS OF THE STUDY

This thesis has aim to assess suicidality in a non-clinical sample during the perinatal period and to report suicidality rates in women with major and minor depressive episode (Mmd) during pregnancy and the postpartum period.

METHOD

Participants

A sample of pregnant women was recruited as part of a larger study conducted at Pisa in the framework of the Perinatal Research and Screening Unit Study (PND-ReScU) *(*Borri, Mauri, Oppo et al*.)*. The PND-ReScU is based on an ongoing collaboration between the Department of Obstetrics and Gynecology and the Department of Psychiatry, Neurobiology, Pharmacology, and Biotechnologies of the *Azienda Ospedaliera Universitaria Pisana.*

The primary aim of the PND-ReScU is to evaluate the effectiveness of screening for early identification and the intervention strategies to reduce mood disorders in the perinatal period. Furthermore, PND-ReScU aims to define a battery of instruments that can be easily administered in a primary prevention setting. Women presenting at the obstetrics/gynecology department for the first ultrasound examination (between the 12^{th} and 15^{th} gestational weeks) were recruited for the study. Central to our recruitment plan was a letter to be given to each pregnant woman who came to the local health service to receive a booklet of information prepared by the region of Tuscany that describes various aspects of pregnancy and maternal health. The letter provides a very brief description of perinatal depression and informs the woman of the possibility of participating in a study aimed at evaluating risk factors for this condition. Study recruitment began in February 2004 and ended in March 2007. To be included in the study, a woman had to be between the 12^{th} and the 15^{th} gestational weeks, be willing to sign an informed consent statement and be available to be contacted by phone. Exclusion criteria for the study were age $\leq$18 years, poor knowledge of the Italian language or other limitations to communication and no fixed residence. The Ethics Committee of the *Azienda Ospedaliera Universitaria Pisana* approved the study protocol and the assessment procedures. The Committee also required the provision of psychological counseling for women with mild depressive symptomatology and/or for all women who requested it and/or the provision of drug treatment for women with moderate/severe depression, according to international guidelines (U.S. Food and Drug Administration, 1979; American Academy of Pediatrics, 2000). All subjects provided written informed consent to

participate in the study after receiving a full description of the study and having an opportunity to ask questions. The Ethics Committee allowed us to collect information only after the informed consent statement was signed, as prescribed by Italian law (art. n. 675 of December 31, 1996) on privacy. Therefore, socio-demographic characteristics of women who refused to participate in the study are not available. The study was funded by a grant from the Italian Ministry of Health.

Assessment Instruments

Several instruments were administered to evaluate a broad range of different aspects related to the perinatal period that might represent potential risk factors for the development of PND. The assessment instruments administered at each time point are listed in Appendix (First et al., 1995; Cox et al., 1987; Beck, 2002; Weissmann et al., 2000; Spielberger, 1983; Dell'Osso et al., 2002; Shear et al., 2001; Dell'Osso et al., 2002b; Cassano et al., 1997;1998). The schedule of assessment is described in Table 1.

The diagnostic assessment was conducted at baseline using the *Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I)* (First MB et al., 1995) by clinicians trained and certified to the use of the interviews when high levels (>0.90) of inter-rater reliability of their diagnoses with the trainer were achieved. All interviewers had long-standing experience in the administration of standardized interviews. The SCID-I is a semi-structured interview for making the major Axis I DSM-IV diagnoses (American Psychiatric Association, 1994). The SCID encompasses the DSM-IV sections for mood, psychotic, sub-stance use, anxiety, somatoform, eating, and adjustment disorders. Moreover, because the clinical and functional impairment related to depressive symptoms often required a therapeutic intervention, we decided to note the categories of partial remission of major depressive episode, (American Psychiatric Association, 1994) which includes women who had a recent major depressive episode and who currently had residual symptoms, and minor depression (Jardri R et al., 2006). The diagnosis of minor depression proposed in the appendix to the DSM-IV (American Psychiatric Association, 1994) requires the presence of 2 to 4 criteria of depression, lasting for at least 2 weeks, excluding individuals with a previous history of MDD (American Psychiatric Association, 1994). For the purpose of this study, we included in this category women who currently met the criteria for the diagnosis of minor depression and who fully remitted from a past episode of major depression, excluding the possibility that this episode was a residual phase of a major depressive episode.

Symptoms of maternal depression were assessed using the 10-item *Edinburgh Postnatal Depression Scale* (Cox et al., 1987). Originally designed as a screening

instrument for postnatal depression, the EPDS has since been validated for use during pregnancy (Murray and Cox, 1990). The EPDS (see Appendix) is a 10-item self-report scale designed as a screening instrument for postnatal depression but has also been validated in non-postnatal women (Cox et al., 1987). Each item is scored on a four-point scale (0–3), the minimum and maximum scores being 0 and 30, respectively. Five of the items explore dysphoric mood, two explore anxiety and three assess guilt and suicidal thoughts. The total is calculated by summing up the item scores. A score of 13 and above is used to identify probable cases with a sensitivity of 86% and a specificity of 78% (Cox et al., 1987). The scale does not provide a clinical diagnosis of depression, but a score above 13 is widely used to indicate the presence of probable depressive disorder. The EPDS rates the intensity of depressive symptoms present over the previous 7 days (see Appendix for a description of the items). A cut-off score of 13 has been found to identify most seriously depressed women, although in case of a score of 9 or more, clinical assessment has been recommended (Cox et al., 1983). In 1992, the EPDS was translated into Italian and was found to have good psychometric properties (Carpiniello et al., 1997). When women exceeded the threshold score (total scores ≥13) of EPDS, suggesting the probable presence of depression, we have re-administered section A of SCID to confirm the diagnosis of depressive disorders. Scores on EPDS item 3, "*blamed myself unnecessarily*", item 4, "*anxious or worried for no good reason*", and item 5, "*scared or panicky for no very good reason*", were extracted for further analysis. These items were clustered as "Anxiety EPDS". Scores on EPDS item 1, "*I have been able to laugh and see the funny side of things*", item 2, "*I have looked forward with enjoyment to things*", and item 8, "*I have felt sad or miserable*", were extracted for further analysis. These items were clustered as "Depression EPDS".

Information on socio-economic status was drawn from the *Postpartum Depression Predictors Inventory-Revised* (PDPI-R) (Beck, 2002), which is a self-report instrument designed to identify the risk factors for postpartum depression. The PDPI-R categorizes socio-economic status on 3 levels: -low, medium, and high, without providing anchor points related to the income per year. The 13 PDPI-R factors are (1) marital status, (2) socio- economic status, (3) self-esteem, (4) prenatal depression, (5) prenatal anxiety, (6) unwanted/unplanned pregnancy, (7) history of previous depression, (8) social support, (9) marital dissatisfaction, (10) life stress, (11) childcare stress, (12) infant

temperament, and (13) maternity blues. The first 10 predictors comprise the prenatal version of the PDPI-R. The last 3 risk factors are specific to the postpartum period. The total score on the prenatal version of the PDPI-R ranges between 0 and 32, while the PDPI-R Full Version (Prenatal plus Postpartum Versions) is used after delivery and includes all 10 factors of the Prenatal Version plus three additional risk factors: childcare stress, infant temperament and maternity blues. The total score of the Full Version ranges between 0 and 39 (Beck et al., 2006). The higher the score, the more risk factors for PPD a subject has. A previous study (Oppo et al., 2009) found that at the 3rd month of pregnancy women who crossed the threshold of 4 had a greater likelihood of having postpartum depression. All the described instruments proved to have good reliability and validity.

The family history of psychiatric disorders was assessed using the *Family History Screen* (FHS) (Weissman et al., 2000). The FHS is used to assess the presence of 15 psychiatric disorders and suicidal behavior in first-degree relatives. The validity of this instrument against best-estimate diagnosis based on direct interview of probands and relatives has been demonstrated for major depression, anxiety disorders, substance use disorder and suicide attempts (Weissman et al., 2000).

The Mood Spectrum Self-Report (MOODS-SR) both the lifetime and the last-month version was also administered (Dell'Osso, Armani, Rucci et al., 2002). This self-report instrument, derived from the corresponding structured interview (Fagiolini, Dell'Osso, Pini et al., 1999), explores features associated with mood disorders.

It focuses on the presence of manic and depressive symptoms, traits and lifestyles that may characterize the "temperamental" affective dysregulations that make up both fully syndromal and subthreshold mood disturbances. The MOODS-SR consists of 161 items coded as present or absent for 1 or more periods of at least 3 to 5 days through the subject's lifetime. The lifetime version include either isolated or clustered symptoms and traits throughout individual's lifetime. The last-month version of the MOODS-SR, that includes the same items as the lifetime version but refers to the month preceding the index assessment, was also administered at study baseline.

Assessment of Suicidality

Suicidality was defined to include thoughts of death or self-harm and suicide attempts and it was investigated by using 2 different sources of information:

1. First outcome measure: Current suicidality was assessed by using item 10 of the EPDS, which investigate thoughts of self harm occurring in the week before the assessment. Women who reported that 'The thought of harming myself has occurred to me' were defined has having suicidality (Evans, Heron, Francomb et al., 2001; Luoma, Tamminent, Kaukonen et al., 2001).

2. Second outcome measure: Current suicidality was explored by 6 questions of the MOODS-SR last-month version inquiring whether the subject has experienced in the last month (independently of a depressive episode) periods of 3 to 5 days or more when she (1) felt like life was not worth living, (2) hoped to die, (3) wanted to die, (4) made suicide plans, and two questions asking whether she actually committed a suicide attempt and whether medical attention was required after the attempt.

Women who endorsed at least one of the six items of suicidality of the MOODS-SR were defined has having suicidality.

Previous suicide attempt assessed with an item of MOODS-SR lifetime version in which "Did you ever try to kill yourself?" was asked.

RESEARCH

To assess suicidality in a non-clinical sample during the perinatal period and to report suicidality rates in women with major and minor depressive episode (Mmd) during pregnancy and the postpartum period.

METHODS

Setting and participants.

The present study was conducted in the framework of PND-ReScU.

The settings for this study were the Department of Obstetrics and Gynaecology and the Department of Psychiatry of the AOUP. All pregnant women presenting at the Department of Obstetrics and Gynaecology for the 1st ultrasound control were potentially eligible for the study. In the first phase of the recruitment, an obstetrician explained the aims of the study, and asked women if they were willing to participate. Women who agreed to be contacted by signing a consent form received a phone call from study personnel to schedule the baseline assessment.

To be included in the study, a woman had to be between the 12th and the 15th gestational week, willing to sign an informed consent form and available to be contacted by phone. Exclusion criteria for the study were: age <18 years, poor knowledge of the Italian language and no fixed residence.

The Ethics Committee of the AOUP approved the study protocol and the assessment procedures. The Committee also required the provision of psychological counselling for women with mild depressive symptomatology and/or for all women who requested it, and/or the provision of drug treatment for women with moderate/severe depression, according to international guidelines (Committee On Drugs, 2000; Food and Drug Administration, 1979).

The Ethics Committee allowed us to collect information only after the informed consent form was signed, as prescribed by Italian law (art. n. 675 of December 31, 1996) on privacy. As such, the socio-demographic characteristics of women who refused to participate in the study are not available.

All women signed an informed consent form approved by the AOUP Ethical Committee and did not receive reimbursement for their participation in the study.

Of the 2,598 women who were asked to participate in the study, 399 (13.5%) did not meet inclusion criteria and 61 (2.3%) miscarried before the baseline assessment. A total of 1,072 (50.1%) refused to participate for various reasons including lack of time, lack of interest in the study protocol, the convictions that they would never become depressed or resistance on the part of the partner. Of those eligible (N=2138), 1,066

(49.9%) signed an informed consent to participate in the study.

Assessment Instruments

The diagnostic assessment was conducted at baseline using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) (First, Spitzer, Gibbon et al., 1995) by clinicians trained and certified to the use of the interviews when high levels (>0.90) of inter-rater reliability of their diagnoses with the trainer were achieved. All interviewers had long-standing experience in the administration of standardized interviews. The SCID-I is a semi-structured interview for making the major Axis-I DSM-IV diagnoses (American Psychiatric Association, 1994). The SCID encompasses the DSM-IV sections for mood, psychotic, substance use, anxiety, somatoform, eating and adjustment disorders.

The Edinburgh Postnatal Depression Scale (EPDS) (Cox, Holden, Sagovsky, 1987) is a 10-item self-report scale, specifically designed to screen for postnatal depression; items are scored on a 4-point Likert scale (from 0 to 3), and the total score ranges from 0 to 30. The scale rates the severity of depressive symptoms experienced over the previous 7 days. Five of the items explore dysphoric mood, two explore anxiety and three assess guilt and suicidal thoughts. The total is calculated by summing up the item scores. A score greater than 12 was used to identify probable cases of depression with a sensitivity of 86% and a specificity of 78%. The EPDS has been also validated for use during pregnancy. The Italian version of EPDS had a good internal consistency (Chronbach's alpha = 0.747) and a sensitivity of 0.556 and a specificità of 0.989 was associated to a score of 12.

The Mood Spectrum Self-Report (MOODS-SR) both the lifetime and the last-month version was also administered (Dell'Osso, Armani, Rucci et al., 2002). This self-report instrument, derived from the corresponding structured interview (Fagiolini, Dell'Osso, Pini et al., 1999), explores features associated with mood disorders.

It focuses on the presence of manic and depressive symptoms, traits and lifestyles that may characterize the "temperamental" affective dysregulations that make up both fully syndromal and subthreshold mood disturbances. The MOODS-SR consists of 161 items coded as present or absent for 1 or more periods of at least 3 to 5 days through the subject's lifetime. The lifetime version include either isolated or clustered symptoms and traits throughout individual's lifetime. The last-month version of the MOODS-SR, that includes the same items as the lifetime version but refers to the month preceding

the index assessment, was also administered at study baseline.

Procedure

Assessments were carried out at the 3rd the 6th and the 8th month of pregnancy, and at the 1st, 3rd, 6th, 9th and 12th month after delivery at the outpatient section of the *AOUP* Gynaecology Clinic.

Statistical analyses

Data are presented as percentages with 95% confidence intervals.

The point prevalence of suicidality was calculated as the percentage of women who reported suicidality with the MOODS-SR last-month version and/or with the EPDS at the 3rd, the 6th, the 8th month of pregnancy and at the 1st, 3rd, 6th, 9th, and 12th month postpartum. The period prevalence of suicidality was calculated as the percentage of women who reported suicidality at any time during pregnancy (3rd to 8th month of pregnancy) and in the postpartum period (1st to 12th month post-partum).

Point prevalence of suicidality were compared across the perinatal assessments using the Cochran's Q. Data were adjusted for multiple comparison.

Odds ratios with 95% confidence intervals were used to measure the association between perinatal depression and sociodemographic and clinical characteristics.

Furthermore, the relationship between the sociodemographic and clinical variables and the occurrence of postpartum suicidality (period prevalence) was analyzed using stepwise logistic regression models adjusting the results for age, previous suicide attempts and lifetime suicidality. All statistical analyses were conducted using SPSS, release 15.

RESULTS

Demographic characteristics of the sample

Of the 2138 women eligible, 1066 (49.9%) signed an informed consent form to participate in the study and completed the baseline evaluation. A total of 1072 (50.1%) refused to participate for various reasons including lack of time, lack of interest in the study protocol, the convictions that they will never become depressed or resistance on the part of the partner.

Mean age of the sample was 32.3 years (SD 3.9), the majority (89.9%) had ≥13 years of education, 92% (N = 981) were married or living with the partner, 82.3% were employed outside the home, 96.2% living in urban or suburban areas and 90.8% had a medium socio-economic status. One third of women (N = 360) had one or more children.

For more details of characteristics on study population see Borri et al. (Borri, Mauri, Oppo et al., 2008) and Banti et al. (Banti, Mauri, Oppo et al., 2010).

Overall 500 women completed the assessment at the 12th month after delivery. During the follow-up, 566 of the 1066 participants who completed the baseline evaluation dropped out (53.1%). Socio-demographic and clinical characteristics were compared between the 566 women who dropped out and those who completed the 12th month follow-up assessment (n=500): no significant differences were detected on marital status, socioeconomic status, educational level, living area and parity. Women who dropped out were significantly younger (31.8±4.1 vs. 32.8 ±3.8; t=3.82; p <0.001), and more frequently unemployed (8.6% vs. 4.5%; chi-square=7.01; p=0.008).

Prevalence of suicidality in the perinatal period

Overall 65 women reported suicidality assessed with the MOODS-SR during the study. The point prevalence of suicidality is presented in figure 2. During pregnancy, the point prevalence of suicidality reached the highest value at the 6th month of pregnancy (3.3%; 95%CI:2.7-3.9). In the postpartum, the point prevalence was higher at the 3rd months postpartum (1.8%; 95%CI:1.2-2.4) than the other assessments (figure 2). However, the point prevalence of suicidality was substantially stable across all the perinatal period (Cochran's Q=12.63, p=0.08). Regarding the period prevalence, defined as the percentage of women who endorsed item of suicidality at any time during pregnancy and in the postpartum period, our results showed that during pregnancy it was 6.9% (95%CI: 6.0-7.8) and during the postpartum period it was 4.3% (95%CI: 3.4-5.2).

Assessing suicidality with item 10 of the EPDS we found that 121 women reported of having at least sometimes "thoughts of self harm occurring in the week before the assessment" during the study. The point prevalence of suicidality ranged from 5.4% (95%CI: 4.7-6.1) at the 3rd month of pregnancy to 3.0% (95%CI: 2.4-3.6) at the 8th month of pregnancy. In the postpartum period it ranged between 2.7% (95%CI: 2.1-3.3) at the 1st months postpartum and 1.2% (95%CI: 0.5-1.9) at the 12th month postpartum (figure 3) . It can be observed that the point prevalence of suicidality assessed with the item 10 of the EPDS significantly decreases from the 3rd month of pregnancy to the other assessments throughout the perinatal period (Cochran's Q=15.88, p=0.026). The period prevalence of suicidality during pregnancy was 12.0% (95%CI: 10.8-13.2) and 8.6% (95%CI: 7.4-9.8) in the postpartum period.

Overlap between suicidality assessed with item 10 of the EPDS and with the MOODS-SR was found in 23 women during pregnancy and in 9 women during the postpartum period (figure 4). Considering women who endorsed suicidality assessed with the EPDS during pregnancy (N=82), the overlap with suicidality assessed with the MOODS-SR was found in 23 women (23/82, 28%). During the postpartum period 36 women reported suicidality assessed with the EPDS, of those, the 25% (9/36) endorsed suicidality with the MOODS-SR.

Considering women who endorsed suicidality assessed with the MOODS-SR during pregnancy (N=49), the overlap with suicidality assessed with the EPDS was found in 23 women (23/49, 46.9%). During the postpartum period 18 women reported suicidality assessed with the MOODS-SR, of those, the 50% (9/18) endorsed suicidality with the EPDS.

Sociodemographic and clinical characteristics associated with suicidality

To determine correlates of suicidality both during pregnancy (period prevalence) and during the postpartum period (period prevalence), we have calculated odds ratios (ORs) of suicidality as a function of age, parity, marital status, educational level, socioeconomic status, employment, a current diagnosis of an axis I disorder, a previous history of an axis I disorder, and a current diagnosis of a minor or a major depressive episode (mMD), using univariate analyses. We calculated ORs with univariate analyses for every correlate of suicidality both during pregnancy and during the postpartum using MOODS-SR (table 1) and item 10 of the EPDS (table 2).

Subsequently, four stepwise logistic regression models were fitted including the age, previous suicide attempts and lifetime suicidality in the models to control for its possible effect. In the first model, a positive association was found between a minor or major depressive episode during pregnancy (OR 6.93; 95% CI 3.52–13.63) and lifetime suicidality (OR 5.88; 95% CI 2.89–11.98) and the suicidality during pregnancy assessed with the MOODS-SR. In the second model, a positive association was found between a minor or major depressive episode during pregnancy (OR 4.51; 95% CI 2.58–7.88), lifetime suicidality (OR 4.15; 95% CI 2.35–7.33) and a low educational level (OR=2.01; 95%CI:1.01-4.01) and the suicidality during pregnancy assessed with the item 10 of the EPDS. Unemployment that was associated with suicidality assessed with the EPDS in the univariate analyses (table 1) were not further associated in the logistic regression model.

Using the postpartum period prevalence of suicidality, we found that having a minor or a major depressive episode during pregnancy (OR=6.76, 95%CI: 2.08-28.32), a minor or a major depressive episode during the postpartum period (OR = 7.62 95%CI: 2.05-

28.32), and lifetime suicidality (OR 4.28; 95% CI 1.19–15.44) were associated with higher odds of reporting suicidality assessed with MOODS-SR, while having a minor or a major depressive episode during the postpartum period (OR = 8.2595%CI: 3.32-20.50) and having a minor or a major depressive episode during pregnancy (OR=2.81, 95%CI: 1.07-7.04), were the only variables associated with suicidality assessed with the item 10 of the EPDS.

Major or minor depression (MmD) and suicidality in the perinatal period

The prevalence of suicidality in women who had a MmD during pregnancy was 26.4% (N=24) and 34.1%(N=28) assessed with the MOODS-SR and the EPDS respectively while the prevalence of suicidality in women who had a MmD during the postpartum period was 18.4% (N=9) and 30.6% (N=15) assessed with the MOODS-SR and the EPDS respectively.

DISCUSSION

This study aimed to assess women's suicidal ideation during the entire perinatal period that, according to a recent paper of Condon (CONDON, 2010) who proposed a "wish list" of women's mental health for the DSM V, comprise the whole pregnancy and the 1st year postpartum.

Our results indicate that the period prevalence of suicidality during pregnancy was 6.9% (95%CI: 6.0-7.8) using the MOODS-SR and 12.0% (95%CI: 10.8-13.2) using the EPDS while the period prevalence of suicidality during the postpartum period was 4.3% (95%CI: 3.4-5.2) and 8.6% (95%CI: 7.4-9.8) using MOODS-SR and EPDS, respectively.

Looking at confidence intervals, our results showed that the prevalence rates of suicidality assessed with the EPDS were significantly higher than those assessed with the MOODS-SR, both during pregnancy and in the postpartum period. Moreover, our results pointed out that the prevalence rates of suicidality were significantly higher during pregnancy than during the postpartum period.

Our results probably reflect our previous research in which we found that the prevalence rate of major or minor depression was higher during pregnancy (12.4%) than during the postpartum period (9.6%) (Banti, Mauri, Oppo et al., 2010; in press). However, it is possible that our data might be biased by a treatment effect because, as required by our Ethical Committee, depressed women were given psychological counselling and/or drug treatment if necessary and followed throughout the entire course of the study. Unfortunately, we can not compare our period prevalence because there are no studies who had considered it.

Nevertheless, looking at every single point prevalence during the postpartum period, we found that our data are in line with those reported by Lindhal et al. (Lindahl, Pearson, Colpe, 2005) who reported that the percentage of women endorsing some thoughts of self harm 4–6 weeks postpartum ranged from 0.5% to 3.7% (Lindahl, Pearson, Colpe, 2005). However, we found lower percentage for all the perinatal period point prevalence than those reported by Evans et al. (Evans, Heron, Francomb et al., 2001) who stated that, using EPDS, the point prevalence of suicidality were 10.2% at the 3rd month of pregnancy, 6.8% at the 8th month of pregnancy and 5.4% at the 2nd month in the postpartum period. It also should be noted that regarding to the prevalence

of thoughts of self-harm and suicidal ideation in the postpartum, rates vary according to the timing of the assessment and/or sample characteristics (Lindahl, Pearson, Colpe, 2005).

In our study a current minor or major depressive episode was associated with suicidality during pregnancy assessed both with the EPDS and with the MOODS-SR; however a low educational level was associated only with suicidality assessed with the EPDS.

Regarding to the postpartum period, an increased likelihood of reporting suicidality was found in women who had a minor or a major depressive episode during pregnancy and who had a minor or a major depressive episode during the postpartum period. Both for pregnancy and postpartum suicidality correlates, we found results in line with the literature that found that 12-month DSM-IV disorders were strong predictors of 12-month suicide ideation (Borges, Nock, Haro Abad, 2010; in press).

Focusing on our second aim, in which we intended to assess suicidality in women with major and minor depressive episode (mMD) during pregnancy and during the postpartum period, we found prevalence rates lower in respect to those reported in women with unipolar depression (54%) (Sokero, melartin, Rytsala et al., 2003). Our results are consistent with Manber et al. (2008) who compared depressed women during pregnancy and depressed women not in pregnancy and found that suicidality assessed with HDRS was significantly lower during pregnancy.

A number of limitations of this study should be considered. First, the sociodemographic characteristics of the women who refused to participate to the study are not available because data collection was possible only after the informed consent form was signed, as prescribed by the Italian law on privacy. A second limitation was that over half of the participants (53.1%) did not complete the follow-up. The third limitation is the homogeneous socioeconomic status of our sample, including predominantly employed women (82.3%) with a medium socioeconomic status (90.8%). Moreover, all women who have required it, had the possibility to receive psychological counselling and/or a drug treatment and to be followed through the entire pregnancy and the first year postpartum. This may account for the lower prevalence rates of suicidality.

Finally, we observed only a partial overlap between suicidality assessed with the MOODS-SR and suicidality assessed with the EPDS.

We may hypothesize that EPDS assess more specifically self-harm behaviors rather than suicidality per se.

In summary, these findings suggest that although suicidality might be lower in this population, a special attention to suicidal ideation for women who have diagnoses of perinatal depression is crucial as part of any screening program.

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Table 1 Sociodemographic and clinical characteristics associated with pregnancy and postpatum suicidality (assessed with MOODS-SR)

	SUICIDALITY DURING PREGNANCY OR (95% CI)	SUICIDALITY IN THE POSTPARTUM OR (95% CI)
MARRIED COHABITING	1	1
NOT MARRIED/COHABITING	2.06 (0.88-4.80)	2.09 (0.59-7.42)
MEDIUM/HIGH EDUCATIONAL LEVEL	1	1
LOW EDUCATIONAL LEVEL	2.12 (0.95-4.72)	0.59 (0.07-4.51)
MEDIUM/HIGH SOCIOECONOMIC STATUS	1	1
LOW SOCIOECONOMIC STATUS	2.19 (0.63-7.68)	1.68 (0.21-13.46)
NULLIPARITY	1	1
MULTIPARITY	1.36 (0.77-2.4)	0.89 (0.36-2.22)
EMPLOYMENT	1	1
UNEMPLOYMENT	1.35 (0.46-3.92)	2.07 (0.45-9.43)
CURRENT AXIS I DIAGNOSIS	**3.51 (1.99-6.18)**	**2.95 (1.15-7.60)**
HISTORY OF PSYCHIATRIC DIAGNOSIS	**2.67 (1.17-6.07)**	2.98 (0.78-11.30)
MDE AT THE 3RD MONTH OF PREGNANCY	**15.78 (6.51-38.23)**	**9.76 (2.43-39.14)**
PREGNANCY MINOR MAJOR DEPRESSION (PP)	**10.69 (5.79-19.74)**	**9.37 (3.55-24.75)**
POSTPARTUM MINOR MAJOR DEPRESSION (PP)		**11.45 (4.30-30.47)**

Table 2 Sociodemographic and clinical characteristics associated with pregnancy and postpatum suicidality (assessed with EPDS item 10)

	SUICIDALITY DURING PREGNANCY OR (95% CI)	SUICIDALITY IN THE POSTPARTUM OR (95% CI)
MARRIED COHABITING	1	1
NOT MARRIED/COHABITING	1.96 (0.97-3.95)	2.36 (0.92-6.02)
MEDIUM/HIGH EDUCATIONAL LEVEL	1	1
LOW EDUCATIONAL LEVEL	**2.90 (1.59-5.30)**	1.26 (0.43-3.75)
MEDIUM/HIGH SOCIOECONOMIC STATUS	1	1
LOW SOCIOECONOMIC STATUS	1.60 (0.53-4.84)	1.85 (0.40-8.56)
NULLIPARITY	1	1
MULTIPARITY	1.47 (0.95-2.30)	0.69 (0.35-1.39)
EMPLOYMENT	1	1
UNEMPLOYMENT	**2.33 (1.14-4.75)**	0.46 (0.06-3.5)
CURRENT AXIS I DIAGNOSIS	**3.19 (2.05-4.97)**	1.58 (0.82-3.06)
HISTORY OF PSYCHIATRIC DIAGNOSIS	1.79 (0.96-3.35)	1.16 (0.46-2.97)
MDE AT THE 3RD MONTH OF PREGNANCY	**17.64 (7.36-42.24)**	**4.27 (1.12-16.28)**
PREGNANCY MINOR MAJOR DEPRESSION (PP)	**5.90 (3.50-9.97)**	**4.83 (2.26-10.31)**
POSTPARTUM MINOR MAJOR DEPRESSION (PP)		**9.37 (4.43-19.81)**

FIGURES

Figure 1 Point and Period prevalence during pregnancy and in the postpartum

(Arrows indicate scheduled assessments of suicidality)

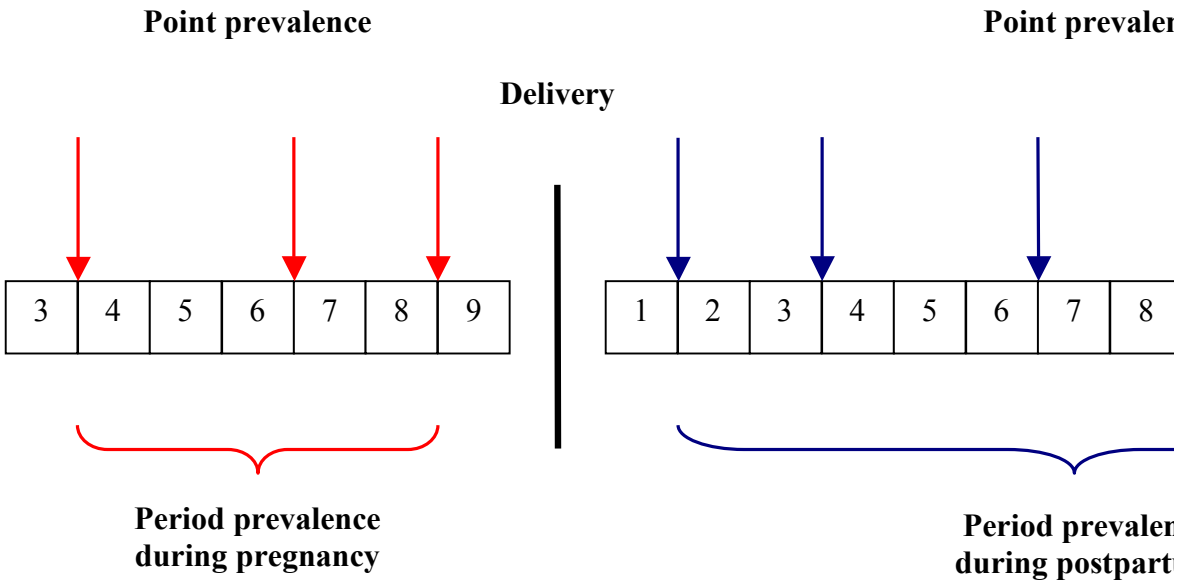


Figure 2 Point prevalence (with 95% confidence intervals) of suicidality assessed with MOODS during pregnancy and in the postpartum

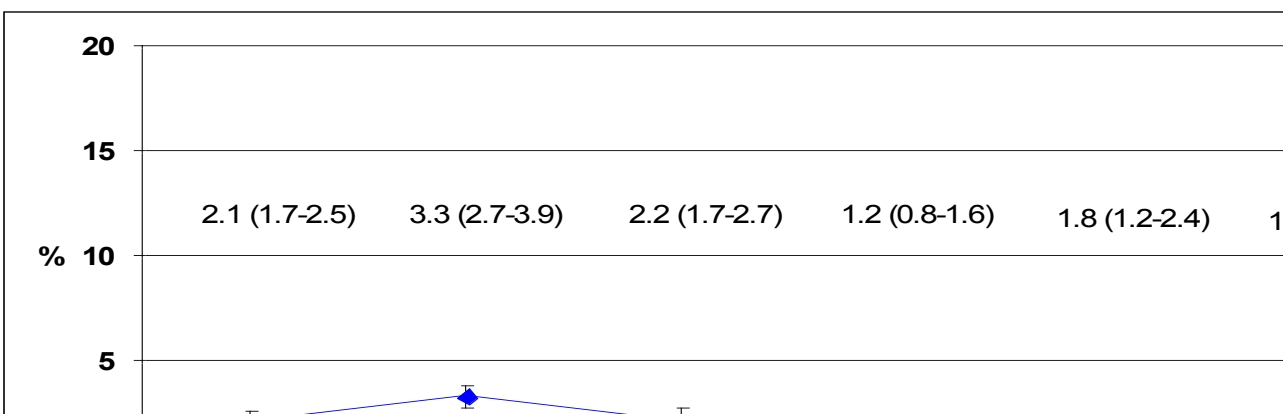
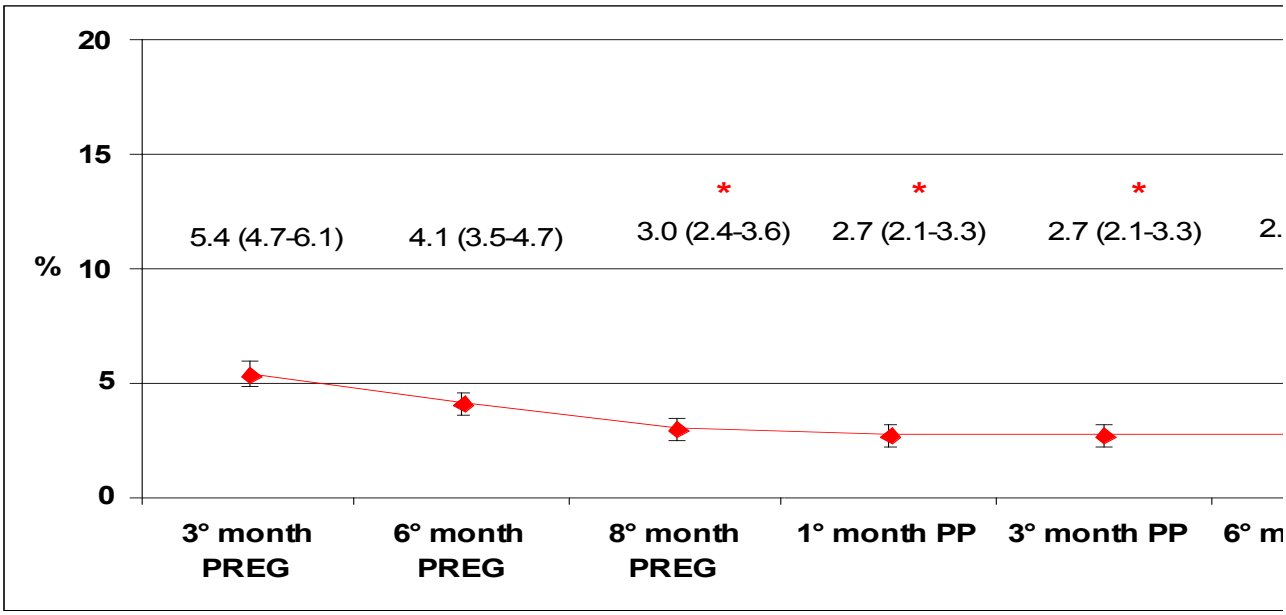


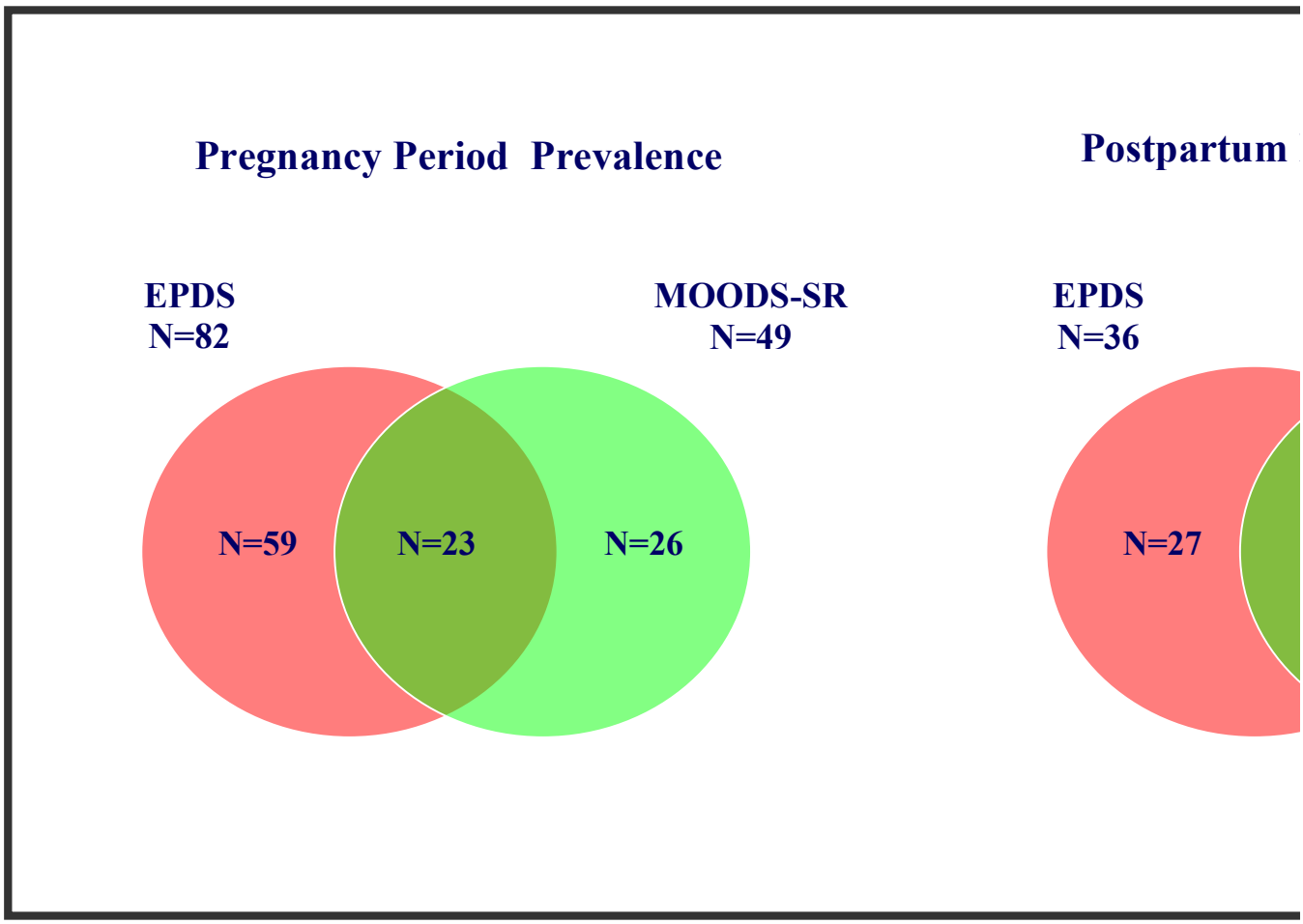
Figure 3 Point prevalence (with 95% confidence intervals) of suicidality assessed with EPDS during pregnancy and in the postpartum



*

*** 3rd month significantly higher**

Figure 4 Overlap between suicidality assessed with the MOODS-SR and with the item 10 of the EPDS


Pregnancy Period Prevalence
Postpartum
EPDS
N=82
MOODS-SR
N=49
EPDS
N=36
N=59
N=23
N=26
N=27

APPENDIX

Instruments

Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) *(First et al., 1995)*
Semi-structured interview for making the major Axis I DSM-IV diagnoses (American Psychiatric Association; 1994). The SCID encompasses the DSM-IV sections for mood, psychotic, sub-stance use, anxiety, somatoform, eating, and adjustment disorders.

Edinburgh Post-natal Depression Scale (EPDS) (Cox et al., 1987)
Ten-item self-report scale, specifically designed to screen for postnatal depression in community samples (Cox et al, 1987), but also validated for use during pregnancy (Murray & Cox, 1990).

Post-partum Depression Predictors Inventory-Revised (PDPI-R) (Beck, 2002)
Instrument that explores 13 risk factors for the development of postpartum depression: the higher the score, the more risk factors a subject has for post-partum depression.

Family History Screen (FHS) (Weissmann et al., 2000)
Instrument that evaluate the familial burden of psychiatric disorders, assessing the presence of 15 psychiatric disorders and suicidal behaviour in first-degree relatives.

Mood Spectrum Self-Report Questionnaire, lifetime version (MOODS-SR-LT) (Dell'Osso et al., 2002)
Instrument that assesses symptoms, traits and lifestyles associated with mood disorders, as well as "temperamental" features related to mood dysregulation; items are organized into 3 manic-hypomanic and 3 depressive domains, as well as a section that assesses disturbance in rhythmicity and vegetative functions, yielding a total of seven domains.

Panic-Agoraphobic Spectrum Self-Report Questionnaire, lifetime version (PAS-SR-LT) (Cassano et al., 1997)
Instrument that consists of 114 items exploring panic-agoraphobic experiences that the subject may have had at any time during their life; in particular: separation sensitivity, typical and atypical panic-like symptoms and agoraphobia, stress sensitivity, medication and substance sensitivity, anxious expectation, illness phobia and hypochondriasis and reassurance orientation.